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The Canadian Medical Association Journal

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WINNIPEG CALLING!

IN this which we call our Convention Number we have endeavoured to concentrate all matter, relevant and irrelevant, pertinent and impertinent, which concerns our Annual Meeting, the only occasion in the year when our Membership has an opportunity to foregather in force. Our readers will be able to glean information about the place of meeting, the program, the entertainment, transportation, accommodation, and much else.

A year or more ago the Executive was in doubt as to the advisability of holding a reunion this year. The cloud of war hung over us and it seemed doubtful whether the sun would break through in time. However, "Business as usual" was adopted as our motto, and it was decided, wisely as we now think, to meet again this year. It was decided, also, again wisely, to convene in Winnipeg. As we write this doubt has given place to hope, and by the time of meeting faith, "the substance of things hoped for", will, we are sure, have been established on a sure foundation. We shall meet, once again, in a hearty, healthy, and friendly atmosphere. But we need your help. Let us all rally to the occasion and GO TO WINNIPEG. The circumstances would seem almost to demand it. We predict a delightful and successful event.

Those of us who had the privilege of being in Winnipeg in 1930, on the occasion of the visit of the British Medical Association to our country, will never forget that gathering. It was hearty, colourful, and inspiring. The hospitality of our hosts knew no limits. To meet our Indian wards and the many races who were to be our new Canadians was a revelation to those of us who hail from "the effete East". It is not, of course, possible that this experience can be repeated, but we can be sure that the hospitality of Winnipeg is not less in this year of grace. It is still as boundless as the prairie, and vastly more agreeable!

We in the East like to feel that we have had some share in the phenomenal growth of the middle and the west of Canada, for did not De La Verendrye, the founder of Winnipeg, hail from Trois Rivières, Quebec. He was the finest type of an adventurer and explorer, and he seems to have left as a legacy something of his dauntless spirit and initiative to his successors in the great city. The future is theirs. We have all heard the rumour that Winnipeg is to be the next capital of the British Empire! When Macaulay's New Zealander sits on a broken arch of London Bridge, gazing on the ruins of St. Paul's, which event, we are all glad to think, is as remote as ever it was, no doubt he will remove to Winnipeg! And, why not?

Next to the foundation of the City the topic of absorbing interest is the Selkirk Settlement and the feud between the Hudson's Bay Company and the Northwest Company. Those who like their history sugar-coated will revel in Frederick Niven's delightful novel, "Mine Inheritance", in which the stirring events of 1812 are portrayed, leading up to the massacre not far from Winnipeg. Court Nez is a great creation. Those who desire a wider horizon will perhaps prefer Lawrence J. Burpee's "The Search for the Western Sea", that will-o'-the-wisp which lured so many of the early explorers to their death. It portrays the numerous expeditions which set forth from the East, South, and North, their fears, their hopes, their struggles, until the quest was won. Winnipeg has a considerable share in the romantic story. Let us plan to meet in Winnipeg. A.G.N.

ON THE USE OF CONCENTRATED POOLED HUMAN SERUM AND POOLED LYOPHILE SERUM IN THE TREATMENT OF SHOCK*

BY BRAM ROSE, PAUL G. WEIL† AND J. S. L. BROWNE

Montreal

THE increasing importance of the problem of shock has stimulated much effort to determine the factors which may be responsible for its production. The question of etiology, however, is still controversial, as some believe that a toxic factor may be the main cause,[1, 2, 28] while others, principally Blalock and his school, are of the opinion that the syndrome may be explained on a basis of fluid loss alone.[3, 4] Still another group feels that a nervous factor may account for the production of symptoms.[5, 31] In contrast to this divergence of opinions, it is generally agreed that, whatever the underlying factor or factors may be, shock is characterized by a loss of plasma volume due to increased capillary permeability,[6] and in the majority of instances by a loss of plasma protein.[7]

The functions of the plasma proteins are of major importance in a consideration of shock and surgical problems in general. The albumin fraction is the most important, for it is the smallest in molecular size and as a result is the first to escape through the capillary wall when permeability is increased. Since the osmotic pressure exerted by a molecule is inversely related to its size it becomes apparent that of all the plasma proteins albumin exerts the greatest osmotic pressure. This is then lowered when albumin is lost and there is a resultant outpouring of fluid into the tissue spaces with the production of œdema. Besides maintaining osmotic equilibrium the proteins of the plasma are of importance in the promotion of active wound healing[8] and in the maintenance of the normal motility of the gastro-intestinal tract.[9] There is also evidence to show that adequate protein stores may inhibit visceral damage such as liver atrophy due to chloroform poisoning.[9]

The plasma proteins are depleted in many types of shock. Working with dogs, Fine and Gendel[10] showed that intestinal obstruction is accompanied by a marked loss of plasma protein when distension is a factor, and this has also been demonstrated in patients.[11] Similar changes have been reported in patients as a result of burns[12] or peritonitis[10] and in experimental shock produced in dogs by cooling of the peritoneum.[13]

Since reduction of the blood volume eventually leads to circulatory collapse the problem of intravenous therapy is of the utmost importance in the treatment of shock. Moon[6] has shown that hæmoconcentration, as evidenced by an increase in hæmoglobin, may precede the fall in blood pressure by as much as three to four hours. It is obvious that valuable time will be gained in establishing a diagnosis if hæmoglobin determinations are made instead of relying on clinical signs and decline of the blood pressure. The value of early treatment is well known, and the clinician has the choice of giving saline, human serum or plasma, or whole blood. Weech and Ling[14] have shown that in patients with moderate hypoproteinæmia, œdema can be produced by the administration of saline. The danger of giving large amounts of saline to surgical patients with hypoproteinæmia has been emphasized by Maddock and Coller[15] and Minot and Blalock.[30] For example, it is not uncommon to administer as much as 3,000 c.c. of normal or 5 per cent glucose saline in a day. This contains 27 g. of salt which is approximately three times greater than the average daily requirement. This can be avoided by carrying out the determination of the hæmoglobin and the plasma proteins, and by giving large amounts of saline only in cases where plasma protein is not diminished, such as in high intestinal obstruction with marked vomiting or in cases where diarrhœa is a factor. As a means of restoring the blood volume, the choice of serum or plasma in preference to whole blood offers many advantages. Both may be kept for much longer periods of time than whole blood without any deterioration. The liquid forms must be kept in the ice-box, but the dried lyophile preparation may be left at room temperature. Either

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† Aided by a grant from the Banting Research Foundation.

may be given at once, since the necessity of typing is obviated and reactions which may occur are not due to incompatibility.[16, 29]

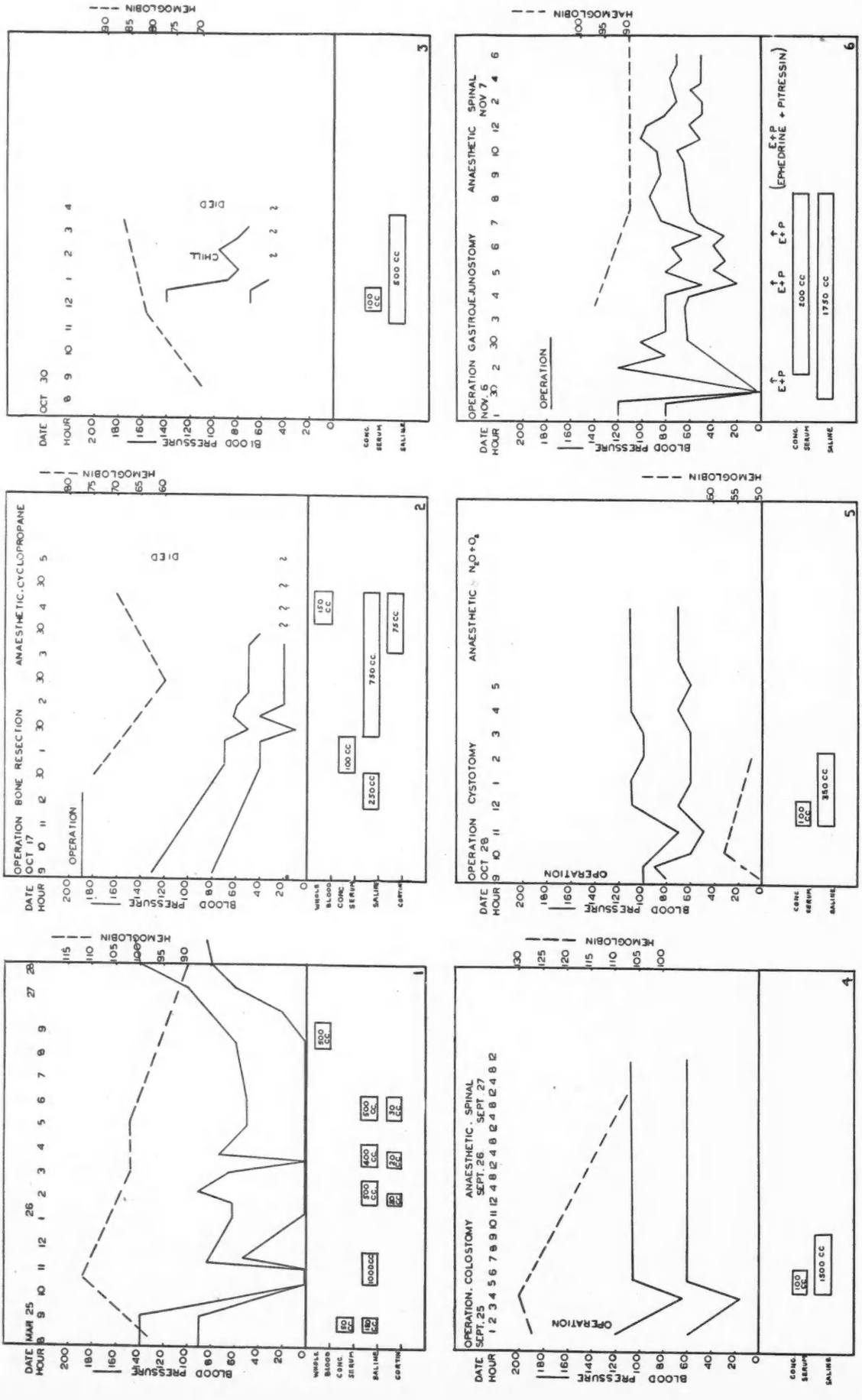
Finally, restoration of plasma volume with serum or plasma does not tend to overburden the circulation with an over-abundance of red blood cells. Even when hæmorrhage has occurred the giving of a small transfusion of plasma or serum immediately may be of great benefit until the patient is typed and whole blood can be administered.

In order to evaluate the efficacy of serum in the treatment of shock and to note the incidence of reactions, two types of pooled serum

TABLE I.

RESULTS OF ADMINISTRATION OF POOLED CONCENTRATED SERUM TO FOURTEEN PATIENTS

No.	*Age*	*Sex*	*Condition*	*In shock when serum administered*	*Amount*	*Reaction*	*Remarks*
1	54	M	Vomiting following gastrectomy. It was thought there might be œdema of stroma secondary to low plasma protein. Total protein 5.7.	No	50 c.c.+ 150 c.c. normal saline	++++	Patient went into profound shock, with hæmoconcentration, low B.P. cyanosis, etc. Recovery.
2	48	M	In shock following bone resection, a long operation with much trauma and considerable hæmorrhage.	Yes	100 c.c. (concentrate)	++++	Patient went into deeper shock with further fall of B.P. coincident with serum. Death.
3	54	M	Bleeding peptic ulcer and thrombosis of femoral artery. Hgb. rose from 70 to 82 in 3 hours before serum was given.	Beginning	100 c.c.+ 500 c.c. normal saline	++++	Chills, cyanosis, drop in B.P. in ¾ hours after serum was begun. Death.
4	40	M	Dehydrated. (Hgb. 127) from diarrhœa of gastrocolic fistula. Operation, colostomy.	Yes	100 c.c.+ 150 c.c. normal saline	....	No reaction. Recovery.
5	63	M	Falling B.P. following supra-pubic cystotomy.	Beginning	100 c.c.+ 350 c.c. normal saline	....	No reaction. Recovery.
6	66	M	Shock following supra-pubic cystotomy; at autopsy — coronary thrombosis.	Yes	100 c.c.+ 250 c.c. normal saline	....	Serum given terminally; no ill effect observed. Death.
7	40	M	Perforated gastric ulcer, generalized peritonitis. Hæmoconcentration marked.	Yes	300 c.c.+ 3,000 c.c. normal saline	....	No untoward effect as far as could be determined. Death.
8	32	M	In shock following spinal anæsthesia. Gastrojejunostomy.	Yes	200 c.c.+ 1,750 c.c. normal saline	....	No untoward reaction. Recovery.
9	45	M	Strangulated hernia, diarrhœa, peritonitis, marked hæmoconcentration.	Yes	450 c.c.+ 3,750 c.c. normal saline	....	Rise in pulse coincident with giving of serum; no untoward reaction observed. Death.
10	50	F	Given serum because of refusal to eat. Patient had renal tuberculosis.	No	150 c.c. (concentrate)	+++	Immediate symptoms, headache, backache, feeling cold, sweating, nausea and vomiting. Recovery.
11	50	M	Bleeding from peptic ulcer.	No	100 c.c.+ 200 c.c. normal saline	....	No reaction. Recovery.
12	24	F	Congestive cardiac failure.	No	50 c.c. (concentrate)	....	No reaction.
13	26	F	Lymphatic leukæmia; given serum (50 c.c.) on September 24th, 28th, 29th and October 31st.	No	50 c.c. (conc.) 50 c.c. " 50 c.c. " 50 c.c. "	++++	Reaction with last serum, chills, feeling of impending death. Recovery.
14	45	F	Burns. Serum given terminally.	Yes	50 c.c.+ continuous saline	....	No untoward reaction. Patient died while serum was being given.


1
OPERATION. COLOSTOMY ANAESTHETIC. SPINAL
SEPT. 25 SEPT. 26 SEPT. 27
OPERATION
2
OPERATION BONE RESECTION ANAESTHETIC: CYCLOPROPANE
OCT 17
OPERATION
DIED
3
CHILL
DIED
4
OPERATION. COLOSTOMY ANAESTHETIC. SPINAL
SEPT. 25 SEPT. 26 SEPT. 27
OPERATION
5
OPERATION CYSTOTOMY ANAESTHETIC N_2O+O_2
OCT 28
OPERATION
6
OPERATION GASTROJEJUNOSTOMY ANAESTHETIC SPINAL
NOV 7
OPERATION
E+P
(EPHEDRINE + PITRESSIN)
DATE
HOUR
BLOOD PRESSURE
HEMOGLOBIN
CONC. SERUM
SALINE

were investigated, both of which were supplied through the courtesy of Professor C. H. Best and the Connaught Laboratories in Toronto. The first preparation was made by placing pooled serum in collodion membranes and concentrating to approximately one-third the original volume by a modified Thalhimer[17] method. The second "lyophile" preparation differed in that the serum was evaporated to dryness from the frozen state.

Where possible a specimen of blood was removed from the antecubital vein before any therapy was instituted. In some cases, when an extensive operation was to be performed, several pre-operative specimens were taken. This offered the advantage of a base line for the interpretation of subsequent results. The blood was kept from clotting by the addition of heparin. All determinations, hæmoglobin, hæmatocrit and plasma protein, were made from the same sample, and all can be done within fifteen minutes. Hæmoglobin determinations were carried out, using the Evelyn photoelectric colorimeter.[18] Although hæmatocrit readings are of value as a check on the hæmoglobin they are not necessary for practical purposes. Scudder[7] has recommended using the specific gravity method for whole blood as a means of following hæmoconcentration. We have tried this method and find that, in comparison with hæmoglobin determinations, it has several disadvantages, in that it is more cumbersome, takes longer to do, and offers a greater probability of personal error. Therefore the use of simple hæmoglobin determinations is recommended in preference as a means of following hæmoconcentration easily and accurately. In the case of hæmorrhage occurring, with unknown quantities of blood loss taking place before the first determination or between two determinations, it is obvious that

Fig. 1. Case 1.—March 25, 1940. Operation: gastrectomy. Because of continued nausea and vomiting it was thought that the patient might have œdema of the stoma secondary to low plasma proteins. To increase his blood proteins he was given 50 c.c. of concentrated serum in 150 c.c. normal saline. As shown by the chart he went into profound shock with hæmoconcentration, cyanosis, sweating, drop in blood pressure, and unconsciousness following the infusion of the serum. March 26, QRS, complexes of very low voltage.

After he recovered from this unfortunate accident the patient's gastric symptom subsided and he was fairly comfortable during the remainder of his stay in hospital. Discharged on April 4, 1940, cured.

Fig. 2. Case 2.—October 17, 1940. Operation: bone resection. In 1915 the patient fractured his left tibia. This fracture was fixed with plate. On October 11, 1940, he sustained a fracture at the site of the plate. Admitted for bone-graft repair.

Operation, October 17, 1940. Cyclopropane anæsthesia from 9 to 11 a.m., during which time the old plate was removed, the bone curetted, and a graft from the left femur prepared. It was estimated that about 500 c.c. of blood might have been lost during these procedures. From 11 to 11.30 a.m. nitrous oxide anæsthesia was given while a plaster cast was applied. Prior to operation his blood pressure was 150/90. A hæmoglobin estimation was not made. When the patient was returned to the ward at 11.30 a.m. he was in shock with cyanosis, cold skin, and unobtainable blood pressure. Saline was immediately given and his blood pressure rose as shown on the chart to 70/40. With the introduction of 100 c.c. concentrated serum his blood pressure fell to 50/10 returned to 65/40, and then gradually declined. During this time the clinical symptoms of shock deepened. Death occurred at 5 p.m. the same day.

Autopsy.—Abdominal viscera appeared normal. No venous engorgement. The stomach was markedly dilated with gas. Heart and lungs normal. Spleen small. Kidneys, liver and adrenals normal. Abdominal parietes pale resembling that seen in hæmorrhage.

Fig. 3. Case 3.—This patient was admitted with a twenty-four hours' history of mild pain and numbness of left leg, vomiting, and bloody stools. An arteriogram showed thrombus of left leg extending above Poupart's ligament. Diagnosis: probable mesenteric thrombosis.

Since he had complained of bleeding and the hæmoglobin had increased from 70 to 82 within three hours he was given intravenous saline and 100 c.c. of concentrated serum slowly. He developed a marked reaction with chills, cyanosis, and a drop in blood pressure about three-quarters of an hour after the serum infusion was started, from which he did not recover.

At autopsy no mesenteric thrombosis was found. There was a duodenal ulcer which had ceased to bleed. There was a femoral thrombosis. No cardiac abnormality present. No cause for immediate death was found.

Fig. 4. Case 4.—September 25, 1940. Operation: ascending colostomy. The patient was admitted for treatment of gastrocolic fistula with diarrhœa. He was markedly dehydrated and emaciated. Within ten days prior to operation (ascending colostomy) he was given seven transfusions to prepare him for the operation. During the operation he went into shock. He was given saline and 100 c.c. concentrated serum, with recovery. No reaction to the serum.

Fig. 5. Case 5.—October 28, 1940. Operation: suprapubic cystotomy. The patient was given 100 c.c. of concentrated serum in 5 per cent glucose saline because of falling blood pressure. No untoward reactions to serum. Recovery uneventful.

Fig. 6. Case 8.—November 6, 1940. The patient went into shock (drop in blood pressure, cyanosis, sweating, restlessness and semi-coma) following spinal anæsthesia (nupercaine). No pre-operative hæmoglobin determination was made so that it is impossible to say whether 97 per cent represents hæmoconcentration, although all subsequent hæmoglobin tests were 90 per cent. He was given ephedrine and pitressin intravenously for the first time as his blood pressure was rising. An intradermal injection, November 9th, of 0.1 c.c. of concentrated serum No. N.C. 512 34-1, July 16, gave no reaction. Recovery uneventful.

neither of these two methods will measure the degree of hæmoconcentration accurately.

The determination of plasma specific gravity on the other hand is a rapid means of ascertaining the amount of plasma protein. A small amount of plasma is all that is necessary and this is readily obtained from the supernatant layer of the hæmatocrit tube. The specific gravity is then determined in the falling-drop apparatus. Once this has been ascertained, it is readily converted into plasma protein using Weech's formula.[19] The apparatus and procedure have been amply described by Scudder.[7]

Hæmoglobin and plasma protein determinations are of great value when considered in relation to each other. If, for example, a fluid approximating the composition of plasma is lost, as is frequently observed in shock due to burns, the protein content of the plasma remains more or less the same, but the hæmoglobin will be markedly increased due to the relative hæmoconcentration. On the other hand, loss of water and salt, such as occurs in high intestinal obstruction with vomiting, leads to an increase in both the hæmoglobin and plasma protein concentration. It is obvious that the former condition would be benefited by plasma transfusion, whereas the latter would require saline.

Results, Using Pooled Concentrated Serum

The first group of patients received concentrated pooled human serum in both the concentrated form and in normal dilution. There were 14 cases in all, and of these 9 were in impending or actual shock when the serum was administered. Of the 14 cases studied, reactions were observed in 5, three of which were very severe. The results are summarized in Table I and details are shown in Figs. 1 to 6. In case 1, not in shock, the administration of 50 c.c. of concentrated serum, made up to normal by the addition of 100 c.c. of normal saline, and of the same type (Universal O) as the recipient's serum was followed by profound shock (see Fig. 1). The serum used in this one case was an earlier preparation not of the pooled type. On the following day 10 c.c. of this serum was injected intravenously into a rabbit. No ill effects were observed. The remaining cases were all given pooled concentrated serum in amounts of 50 to 450 c.c. Three of these received the serum in the undiluted form, whereas in the remainder it was first diluted to normal. Severe reactions were observed in cases 2 and 3 (see Figs. 2 and 3) with death following shortly after administration of the serum. Moderate reactions were observed in two cases (Nos. 9 and 10) not in shock.

Nine of the patients tolerated the serum without any reactions, and of these 7 were definitely improved. The two remaining patients died, one of an acute coronary thrombosis, and the other of peritonitis. An example of the effects of treatment is shown in Fig. 4. This patient (No. 4) went into shock following operation. His hæmoglobin was 130 per cent and the plasma protein was 5.4 g. per cent. He was given 100 c.c. of concentrated pooled serum and 1,500 c.c. of normal saline, and, as will be observed, the blood pressure was restored to normal limits within half an hour. A subsequent hæmoglobin reading (12 hrs.) was 117 per cent, and in 24 hours it was 107 per cent. The plasma protein remained at 5.2 g. per cent, indicating that there was no further loss of protein.

An interesting observation was made in case 13. This patient, with leukæmia, was given 50 c.c. of concentrated serum on September 24th, 28th, and 29th. No reaction was observed. Owing to a delay in obtaining more serum, she did not receive the next injection until October 31st, when she was again given 50 c.c. This was followed by chills, fever, and a fear of death within several minutes. Tests for skin sensitivity to the same batch of serum showed a reaction in concentration of 1 to 100, a slight reaction to fresh serum diluted 1 to 10, and no reaction to normal plasma diluted 1 to 10. This case then raises the question as to whether partial denaturation of the proteins may occur during the process of preparation. If such were the case serious consequences might result since repeated administration of serum may then sensitize a patient to human serum, with the production of a violent reaction upon subsequent administration.

From the results of treatment with concentrated pooled serum in this small group of 14 patients, 5, or approximately 35 per cent, developed reactions which in two instances were followed by death shortly after the administration of the serum (cases 2 and 3). The nature of these reactions is obscure. They occurred irregularly and unpredictably.

RESULTS USING POOLED LYOPHILE SERUM

A second group of 16 patients was given intravenous injections of lyophile serum. Lyophile serum differs from concentrated serum in that it is evaporated down to absolute dryness soon after separation from the blood, the end-product of which resembles brown sugar. It is readily soluble in water and derives the name "lyophile" from this characteristic.

Because of the high percentage of reactions encountered when concentrated serum was administered to patients in shock, it was decided to administer this second type of serum to relatively normal persons or at least to patients definitely not in shock, and the serum was always given in normal concentration.

To a sterile bottle of lyophile serum (representing 300 c.c. of serum) 270 c.c. of pyrogen-free distilled water were added under sterile conditions. Within 10 to 15 minutes it was ready for administration. The pulse, blood pressure, temperature and respirations were followed in all instances at frequent intervals up to six hours. Fourteen patients received one transfusion of 300 c.c. each, and one patient received one transfusion of 550 c.c. In no instance were any severe reactions observed, although minor reactions, which consisted of urticaria in one case, rise of pulse and temperature in another, and a feeling of tightness about the chest in two others, were noted. The last ten transfusions were administered at a rate of 15 c.c. per minute.

DISCUSSION

The striking difference in the results obtained in the use of the two types of serum must be considered in relation to the condition of the groups of patients and the method of preparation of the serums. For example, 9 of the fourteen patients in group one were in shock; in the second group treated with the lyophile preparation, however, all were in relatively good health. It may be that what appears to be a minor reaction in a healthy person could be a severe reaction in a patient who is in shock. Whether this is the case or not will have to be proved by the administration of the lyophile serum to cases of shock; differences in the method of preparation of the two types of serum may also be of importance.

A survey of the recent literature on the use of plasma and serum in the treatment of shock reveals the following facts. Plasma, either unprepared, concentrated, or lyophilized, has been used by a large number of workers, the majority of whom have not observed any untoward reactions. Strumia, Wagner and Monaghan[20] have used normal citrated plasma in a large number of cases with good results. They claim that they had to abandon the use of serum because it gave so many reactions. The same conclusion was reached by Scudder,[21] Fine and Gendel,[10] and by Brennan.[22]

On the other hand, a consideration of the use of serum either in patients or in the experimental animal reveals that with few recent exceptions most workers have observed so-called serum reactions. An incidence of 25 per cent reactions was noted by Levinson, Neuwelt and Necheles.[23] Recently Buttle *et al.*,[24] in a survey of the use of various substitutes for blood in therapy, came to the conclusion that plasma was by far the best, and that serum gave too many reactions.

Best and Solandt[16, 17] have advocated the use of serum in preference to plasma, and have put forward evidence supporting this view both from animal experimentation and administration to human beings. Perhaps the best evidence has been presented by Brown and Mollison[25] who treated 91 cases with either concentrated or normal pooled human serum. They noted 19 reactions (± 20 per cent). Using plasma, they observed somewhat the same percentage (± 26 per cent), and came to the conclusion that either plasma or serum may be used if they are properly prepared. Long[26] treated 21 cases of shock with lyophile serum and observed no reactions.

Apparently, there are advantages in the preparation of serum as compared to plasma. The presence of fibrin and anticoagulant in the latter make evaporation quite difficult.[27] Where transportation and weight are major factors, the lyophile product offers the greatest advantage, and it, furthermore, will remain in good condition at room temperature. For general use in hospital, however, it would seem that removal of plasma from citrated whole blood (previously kept in a bank) offers a simpler and more economical plan.

Although the evidence is still confusing, it is felt that the majority of workers using plasma have in general noted considerably less reactions than those using serum (untreated). Further, the type of reaction observed in case 13 (Group 1) in whom no symptoms occurred until the patient had received several pre-

liminary transfusions of concentrated serum must be considered seriously in the light of Scudder's findings.[21] Using the electrophoretic method of analysis, he noted that changes occurred in the proteins of lyophile serum, whereas none were observed in plasma which had stood for several months.

CONCLUSIONS

Thirteen cases, 5 of whom were in shock, were treated with pooled concentrated human serum, and one additional case received concentrated typed human serum. Reactions to the serum were observed in 5, or 35 per cent, of the cases, and death followed in two of these. In the 9 cases in which no reaction was observed the results of serum therapy were beneficial in seven. Because of the frequency and nature of the reactions it is felt that this type of serum is contraindicated in the therapy of shock.

Sixteen patients, not in shock, were given transfusions of pooled lyophile serum. No severe reactions were observed.

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REFERENCES

1. CANNON, W. B.: *Ann. Surg.*, 1934, **100**: 704.
2. DALE, H. H., RICHARDS, A. N. AND LAIDLAW, R. P.: Special Committee on Shock and Allied Conditions, 1918.
3. BLALOCK, A.: *Arch. Surg.*, 1930, **20**: 959.
4. HOLT, R. L. AND MACDONALD, A. D.: *Brit. M. J.*, 1934, **1**: 1070.
5. SLOME, D. AND O'SHAUGHNESSY, L.: *Brit. J. Surg.*, 1938, **25**: 900.
6. MOON, V. H.: Shock and Related Capillary Phenomena, Oxford University Press, New York, 1938.
7. SCUDDER, J.: Shock; Blood Studies as a Guide to Therapy, Phila., Lippincott, 1940.
8. THOMPSON, W. D., RAVDIN, I. S. AND FRANK, I. L.: *Arch. Surg.*, 1938, **36**: 500.
9. RAVDIN, I. S., STENGEL, A. AND PRUSHANKIN, M.: *J. Am. M. Ass.*, 1940, **114**: 107.
10. FINE, J. AND GENDEL, S.: *Ann. Surg.*, 1940, **112**: 240.
11. GENDEL, S. AND FINE, J.: *Ann. Surg.*, 1939, **110**: 25.
12. ELKINGTON, J. R., WOLFF, W. A. AND LEE, W. E.: *Ann. Surg.*, 1940, **112**: 150.
13. MAHONEY, E. B.: *Ann. Surg.*, 1938, **108**: 178.
14. WEECH, A. A. AND LING, S. M.: *J. Clin. Investigation*, 1931, **10**: 869.
15. MADDOCK, W. G. AND COLLER, F. A.: *Ann. Surg.*, 1940, **112**: 520.
16. BEST, C. H. AND SOLANDT, D. Y.: *Brit. M. J.*, 1940, **1**: 799.
17. *Idem*: *Canad. M. Ass. J.*, 1940, **43**: 206.
18. EVELYN, K. E. AND CIPRIANI, A.: *J. Biol. Chem.*, 1937, **117**: 365.
19. WEECH, A. A., REEVES, F. B. AND GOETTSCH, E.: *J. Biol. Chem.*, 1936, **113**: 167.
20. STRUMIA, M. M., WAGNER, J. A. AND MONAGHAN, J. F.: *J. Am. M. Ass.*, 1940, **114**: 1337.
21. SCUDDER, J.: *Ann. Surg.*, 1940, **112**: 502.
22. BRENNAN, H. J.: *Brit. M. J.*, 1940, **1**: 1047.
23. LEVINSON, S. O., NEUWELT, F. AND NECHELES, H.: *J. Am. M. Ass.*, 1940, **114**: 455.
24. BUTTLE, G. A. H., KEKWICK, A. AND SCHWEITZER, A.: *The Lancet*, 1940, **2**: 507.
25. BROWN, H. A. AND MOLLISON, P. L.: *Brit. M. J.*, 1940, **2**: 821.
26. LONG, A. G. G.: *Brit. M. J.*, 1940, **2**: 915.
27. ALWARD, F. X., MAINWARING, B. R. S. AND WILKINSON, J. F.: *Brit. M. J.*, 1940, **2**: 583.
28. KENDRICK, D. B., JR., ESSEX, H. E. AND HELMHOLZ, H. F., JR.: *Surg.*, 1940, **7**: 753.
29. EDWARDS, F. R., KAY, J. AND DAVIE, T. B.: *Brit. M. J.*, 1940, **1**: 377.
30. MINOT, A. S. AND BLALOCK, A.: *Ann. Surg.*, 1940, **112**: 557.
31. LORBER, V., KABAT, H. AND WELTE, E. J.: *Surg., Gyn. & Obst.*, 1940, **71**: 469.

PROBLEMS IN THE PRESERVATION OF BLOOD

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THE visible changes that occur in blood during storage have been described by many authors, but it may be well to recapitulate them.

Sedimentation of the cellular elements in blood commences almost immediately blood is drawn. The rate varies with different bloods and is influenced by factors such as the composition of the diluent or preservative, which may influence cell volume, and by factors which influence specific gravity and viscosity, as, for example, temperature and the degree to which the blood has been diluted. In most specimens sedimentation of corpuscles is usually fairly complete within 36 to 48 hours. White cells and platelets, particularly the latter, settle out much more slowly, and many break down before sedimentation is complete. Many are entrained by the corpuscles during their sedimentation, the distribution throughout the red-cell mass being greatest at the top and diminishing rapidly as one proceeds downwards. The remaining leucocytes and platelets settle out in the course of a few days to form a thin whitish layer on top of the red cells. Because of the tendency of these elements to agglutinate the layer soon becomes consolidated into a membrane. In centrifuged samples the white-cell layer becomes sufficiently compact to be removable *en masse* with a forceps or by aspiration. If, after a few days' storage, a fragment of the layer be stained and examined under the microscope it may appear as a mat of straight fibrin shreds enclosing the surviving leucocytes and platelets, chiefly lymphocytes. Once consolidation of the white-

cell layer has taken place, it is impossible to disperse the cells individually again by agitation; at best the film may be broken into small fragments. The tendency of white cells and platelets to agglutinate and to form a cohesive membrane appears to be more marked in some species than in others.

It is to be expected that autolytic changes and hence disintegration during storage should occur more rapidly in the nucleated elements. The polymorphonuclear cells begin to break down early and almost completely disappear within seven to ten days. The platelets also are easily destroyed. According to some authors they disappear within a matter of hours or a few days, but our observations agree with those of Dubash, Clegg and Vaughan,[1] that a fair proportion may survive for two or three weeks. Their survival is influenced also by the manner in which blood is collected, the composition of the preservative, and by conditions of storage. Of all the white cells, the eosinophiles and monocytes are the most stable, many surviving six weeks to two months.

The disintegration of leucocytes and platelets in stored samples is indicated by an apparent swelling of the white-cell layer and its becoming "fuzzy", "buffy" or "woolly" in appearance, usually about the tenth to the fourteenth day of storage. Diffusion of free hæmoglobin into the plasma often becomes detectable at that time also. Hæmolysis actually begins quite early in storage, but diffusion of hæmoglobin into the plasma is hindered until the white-cell layer begins to disintegrate. Unless the red cells be resuspended and allowed to settle again the redness of the plasma cannot be taken as a criterion of the condition of the sample.

That hæmolysis during storage is largely the consequence of osmotic changes has been shown by Maizels and Whittaker,[2] who have observed that the corpuscles gradually increase in volume and ultimately burst. In the process of swelling the cell becomes more spheroidal in shape and decreases in its long diameter.[3, 4, 5] Earlier investigators had shown that soon after blood is drawn, the red-cell membrane, which normally is not very permeable to potassium ions and is practically impermeable to sodium, becomes altered so that these ions diffuse freely through it. An equilibrium is never established because, as Maizels and Whittaker[2] have pointed out, the colloid osmotic pressure within the corpuscle, due chiefly to hæmoglobin, is greater than the colloid osmotic pressure of the plasma. Consequently, water continues to enter the cell. The attainment of equilibrium is further interfered with by the continual formation of new ions such as lactate, phosphate and ammonium, together with non-diffusible ones, from autolytic changes during storage.

Other factors may favour hæmolysis by weakening the red-cell membrane, as, for example, the slow liberation of ammonia[2, 6, 7] within the corpusele, and possibly the formation in the plasma of hæmolytic products such as lysolecithin.[8, 9] Many investigators have shown the rapid increase in the fragility of cells in hypotonic saline solutions during storage, but to what extent fragility is attributable to the stretched state of the cell membrane from swelling, or, on the other hand, to lowered resistance of the membrane, has not yet been ascertained. Many substances added to preservative solutions, even in small amounts, tend to make the corpuscles less stable. There is some evidence that the disintegration of white cells and platelets also has an unfavourable influence on the red-cell membrane, possibly by liberation of proteolytic, lipolytic and other enzymes. Defibrination definitely increases the fragility of the corpuscles and it is possible that the gradual formation of fibrin which inevitably takes place during storage also may have a deleterious effect. This question will be discussed in a later report.

The beneficial influence of glucose in retarding hæmolysis was first reported by Rous and Turner[10] in 1916. Studying this action of sugar, Maizels and Whittaker[2] observed that in the presence of glucose the corpuscle is capable of undergoing a greater degree of swelling before hæmolysis occurs. Thus, according to these authors, red cells when placed in hypotonic saline (0.49 per cent) increase about 60 per cent in volume before breaking down, that is, hæmolysis occurs at a "critical cell volume" of 160 per cent of normal. Sucrose enables the cell to increase 72 per cent and glucose 83 per cent in volume before hæmolysis occurs. Other sugars also have a beneficial influence, but their order of merit varies with different bloods. In some instances fructose appears to be better than glucose, while in others sucrose is superior. In the majority of cases, however, glucose is best. Further, it is a more physiological substance. There is still a difference of opinion as to the optimal concentration of glucose.

A survey of the literature reveals little uniformity with regard to preservatives used in blood storage. It is interesting to compare the preferences of various workers in this regard (Table I).

In the past year or so there has been a departure from the use of complex saline preservative mixtures, as employed earlier by the Russian workers. The majority of investigators now use citrate alone or citrate-sodium-chloride mixture with or without glucose. In the experience of some workers, including our group, the addition of sodium chloride to the preservative is undesirable, and optimal results are obtained by using a simple citrate-glucose mixture. Phosphate is of doubtful value, since it accelerates glycolysis and the breakdown of the cell membrane. Valuable observations on the influence of various preservatives may be found in the reports of Dubash, Clegg and Vaughan,[1] of Bushby and co-workers,[11] and others.[2, 12]

TABLE I.

Authors	*Diluent*	*Blood: Diluent*	*Final percentage citrate*	*Citrate percentage on basis of blood*	*Final percentage glucose*
Rous and Turner[10]	Citrate-glucose	3:7	0.76	2.3	2.7
Moscow Institute Hæmatology "I.H.T."[54,66]	"I.H.T." citrate-salt mixture	1:1	0.25	0.5	None
Reed[55]	Citrate-glucose	1:3.4	0.8	2.7	2.7
De Gowin *et al*[35]	Citrate-glucose	1:1.5	0.25	0.64	2.8
Cook County Hospital[17,56,57]	Citrate (2.1%)-NaCl	7:1	0.3	0.3	None
Kings County Hospital[58]	Citrate-NaCl	6:1			None
Elliott *et al*[59]	"I.H.T." citrate-salt mixture	1:1	0.25	0.5	None
Barton & Hearne[60]	"I.H.T." citrate-salt mixture-glucose	1:1	0.25	0.5	2.5
Hamilton-Paterson[61]	Citrate-glucose	4:1	0.63	0.8	2.0
Maizels & Whittaker[2]	Citrate-NaCl	2:1	0.35	0.7	None
Downman *et al*[12]	Citrate-NaCl	2:1	0.52	0.5	None
Aylward *et al*[62]	Citrate-glucose	24:1	0.35	0.35	1.0
Lipp & Hubbard[63]	Citrate	10:1	0.2	0.2	None
Dubash, Clegg & Vaughan[1]		2:1	0.35	0.5	0.1-1.0
Edwards & Davie[64]	Citrate	9:1	0.4	0.4	None
Bushby *et al*[11]	Citrate-glucose	3:1	0.5	0.7	0.34
Brewer, Maizels, Oliver & Vaughan[45]	Citrate-saline-glucose	2:1	0.35	0.5	1.0
Johns Hopkins Hospital[65]	Citrate-glucose	10:1	0.45	0.5	None

The ordinary fragility test affords a useful means of ascertaining changes in the stability of red cells during storage. It has been shown by many workers that from the time blood is taken the corpuscles become progressively less stable to hypotonic saline. After a few days some of the cells become unstable even to normal saline. The rate of increase in fragility can be correlated with changes in the distribution of the electrolytes and with the degree of swelling. According to Parpart,[13] and others,[5] erythrocytes can swell to a volume at which the membrane becomes permeable to hæmoglobin. Hæmoglobin, therefore, may escape from the cell without hæmolysis.

That the red cell membrane becomes permeable to potassium and sodium almost as soon as blood is withdrawn was shown by Dulière[14] and by Jeanneney and Servantie,[15] and has been confirmed by many others. The rate of diffusion of potassium ions from the cell and of sodium into the cell is almost linear for about ten days, after which it becomes progressively slower. There appears to be a relationship between the diffusion of the two ions; in some cases this amounts almost to an ion-for-ion exchange. The rate of diffusion of potassium, however, is slightly greater, as might be expected from its relatively greater mobility. Storing blood under an atmosphere of carbon dioxide diminishes the rate of diffusion of both ions.[16] As shown later and confirmed by other workers,[12] the diffusion of potassium from the cell is slightly greater at lower temperatures. In the study performed by Eisenman and collaborators[18] on the permeability of the erythrocyte to radio-potassium and sodium there was little evidence of exchange between potassium of the cells with potassium added to the serum. Dean and his colleagues,[19] on the other hand, found that the membrane was somewhat permeable to radio-potassium.

The influence of other ions on the diffusion of potassium and sodium has been demonstrated

by Davson[20, 21] in his studies on the erythrocyte of the cat. Thus, anions such as sulphate and citrate at the dehydrating end of the lyotropic series retard the passage of potassium into the cells and accelerate the escape of sodium. On the other hand, ions such as thiocyanate, at the hydrating end of the series, reverse these effects. No detailed studies of the influence of these ions have been made on the human red cell, but doubtless analogous effects would be observed. Since the stability of the corpuscle is markedly affected by osmotic readjustments and particularly by the increase in cell volume due to entrance of water, the importance of studying the influence of other ions is apparent. Investigations of earlier workers on the hæmolytic effect of various ions and their influence on the shift of water through membranes also have an important bearing on the question.

Ions such as phosphate, ammonium, lactate and others, liberated in preserved blood by autolysis, possibly exert a dual influence on the stability of the cell by increasing the osmotic pressure and by altering the permeability of the membrane. The liberation of inorganic phosphate from diphosphoglycerate and organic pyrophosphate has been studied extensively by Rapoport[22] and by Maizels and Whittaker.[2] According to the latter investigators the inorganic phosphate in the plasma is doubled in about two weeks and that inside the corpuscle increases to ten or twenty times the original level. The rate of diffusion from the cell, however, is relatively slow. Eisenman *et al.*,[18] using radiophosphate, have observed that the membrane is permeable to this ion at 38° C. but almost impermeable at 7° C., thus confirming the observation of Maizels.[2] Liberation of phosphate within the cells should therefore tend to attract water and promote swelling. Ammonia is liberated slowly in the erythrocyte, presumably from breakdown of adenosine and adenylic acid.[6, 7] According to Maizels and Whittaker[2] it increases from the normal concentration of 0.3 mg. per cent to about 5 mg. per cent in about seven weeks. The breakdown of the nitrogenous constituents of the cell, therefore, is relatively slow, and may further be retarded by storing blood under carbon dioxide.[6, 16] From what has been said regarding the diffusion of phosphate, and from the observation made by the writers and others that the diffusion of potassium from the corpuscle is more rapid at low temperatures, it is apparent that temperature may determine as well as regulate permeability.

Hæmoglobin.—The stability of hæmoglobin is a consideration of fundamental importance in the preservation of blood. Two questions arise, namely, how long does hæmoglobin retain its normal oxygen-carrying capacity; and, secondly, how is the rate of oxygenation and dissociation affected by conditions and time of storage? Since hæmoglobin becomes useless after breakdown of the corpuscle these questions apply chiefly to hæmoglobin in the intact cells, and hence are of practical importance only within the useful period of storage.

From the time blood is collected, and particularly after sedimentation is complete, the corpuscles gradually lose oxygen and become venous in colour. They are always darkest at the bottom of the sample and only a shallow layer at the top in contact with the supernatant plasma remains oxygenated. After a few weeks the cells become extremely dark. This change occurs, though in lesser degree, even when samples are stored under oxygen. Apparently the hæmoglobin is not altered, at least within the first few weeks, since on resuspending the corpuscles in the presence of air they readily become oxygenated and assume the characteristic bright red colour. If the red cells are kept in suspension and in contact with oxygen during storage they remain oxygenated for a long time. In the course of two or three months, however, there is a noticeable darkening of the colour. The arterial colour is retained much better when blood is stored in containers with ground-glass stoppers than in rubber-stoppered tubes, thus suggesting that the loss of arterial colour may partly be due to escape of oxygen from the vessel.

The darkening of the colour in stationary specimens suggests several possible causes: (1) loss of oxygen due to instability of oxyhæmoglobin in the presence of increased acidity from glycolysis and other changes; (2) abstraction of oxygen by certain aerobic oxidative processes in autolysis; (3) change in ionic environment rendering oxyhæmoglobin less stable; and (4) deterioration of hæmoglobin with a resulting diminution in oxygen-carrying capacity. It has been shown by Fairley[23] that hæmoglobin tends to change to methæmoglobin during incubation, but this alteration is extremely slow at low temperatures. Another possibility under in-

vestigation at present is the formation of "pseudohæmoglobin", which, according to Barkan and Walker,[24] exists in normal blood and is higher in osmotically less resistant corpuscles, *i.e.*, presumably the older cells. The evidence at the present time indicates that hæmoglobin is quite stable for a long time during storage and that slight differences observed in the rate of oxygenation may be due to the influence of changes in ionic composition[25, 26] within the cell rather than to alteration in hæmoglobin itself.

METHODS

1. *Collection and storage of blood.*—For the collection of blood standard equipment such as the Baxter and Abbott types has been used whenever possible. The collecting procedure, however, has been modified slightly. For obvious reasons, where blood is to be collected in different preservative mixtures the closed method of bleeding is impracticable. The following procedure has been found most satisfactory. The required amount of anticoagulant in isotonic concentration, is placed in the container, and the mouth of the latter is covered with a double sheet of cellophane with a hole (⅜ inch) in the centre large enough to admit the bleeding tube. After tying the cellophane around the neck of the flask the mouth is covered with a heavy pad of gauze, and the flask is autoclaved. Precaution is taken to avoid greatly reduced pressure at the end of sterilization so as to prevent loss of solution through sudden ebullition or of water by evaporation. If glucose is to be added to the preservative it is sterilized separately to avoid caramelization and may be added to the collection flask through the aperture in the cellophane, preferably before bleeding. A slight degree of caramelization has no adverse influence on the stability of the corpuscle during storage, and apparently is not toxic. However, it tends to produce an acid reaction in the solution and should be avoided, particularly when blood is to be used for transfusion.

The diluent or preservative used is a modification of De Gowin's, and is used in the following proportion:

Blood: 5 parts.

Isotonic trisodium citrate (3.2 per cent solution of dihydrate): 1 part.

Isotonic glucose (5.4 per cent solution): 1.5 parts.

The blood is collected without aspiration. The sphygmomanometer cuff is adjusted and the donor's arm sterilized with alcohol and iodine, and covered above and below the antecubital vein with sterile towels. After anæsthetizing the region over the vein with a small injection of procaine, and the donor maintaining the cuff pressure at 80 mm., the needle (short number 13 or 16 with a short curved bevel and with a 7-inch length of stout gum-rubber tubing attached), is inserted and the blood conveyed into the bottle through the cellophane protection. The bottle is usually cooled in the refrigerator beforehand. If blood is to be collected in more than one container it is simple to clamp off the bleeding tube momentarily while the flasks are changed. Finally, the cellophane protection is removed from the bottle and a suitable sterile dispensing stopper or head is applied. The citrated blood may then be dispensed into smaller flasks containing various solutions to be tested, all flasks being protected with perforated cellophane as described above. For serial analysis it has been found convenient to dispense samples into 4-c.c. culture tubes. This ensures sterility and obviates sampling errors and the necessity of disturbing the entire lot of sample when a specimen is required. Aseptic precautions are observed throughout all manipulations. Samples are stored in refrigerators maintained at 4 ± 1° C.

ANALYTICAL METHODS

1. *Fragility.*—Fragility of erythrocytes to hypo- and hyper-tonic solutions of saline was determined by a modification of the method of Waugh and Asherman.[27] Hæmolysis is expressed as grams of free hæmoglobin per hundred ml. of solution, or in per cent of the total hæmoglobin in the sample.

2. *Hæmoglobin.*—Hæmoglobin was estimated colorimetrically by the method of Evelyn,[28] or by the micro method of Wu,[29] adapted for use with the Evelyn photoelectric colorimeter. Hæmoglobin was also estimated on the basis of oxygen-carrying capacity by Van Slyke's manometric method.[30]

3. *Potassium.*—By a modification (O.F.D.) of the silver-cobalti-nitrite method of Zwemer and Truszkowski,[31] adapted for use with the photoelectric colorimeter.

4. *Sodium.*—By a modification (Stansfield and Denstedt) of the zinc-uranyl-acetate method, using the photoelectric colorimeter.

5. *Sugar.*—By Somogyi's[32] modification of the method of Shaffer and Hartman.

6. *Chlorides.*—By a micro modification of the method of Wilson and Ball.[33]

EXPERIMENTAL

Fragility of corpuscles during storage.—The isotonic buffered Simmel's solution as used by Waugh and Asherman was adjusted to pH 7.35. From this solution dilutions were made so as to give a hypotonic series represented by 30, 40, 50, 60, 70, 80 and 90 per cent respectively, of isotonic. Hypertonic sodium chloride solutions represented by 200, 300 and 400 (per cent of isotonic), respectively, were also prepared.

Fragility was determined by adding 0.02 ml. of blood to 10 ml. of each solution in the above series in colorimeter tubes. After five minutes the tubes were centrifuged to throw down any unhæmolysed cells, and the free hæmoglobin in the supernatant fluid was estimated colorimetrically. A complete fragility curve was usually done on samples as soon as collected, and tests were made periodically thereafter, using test solutions 0 (water) 70,100 and 300. Table II illustrates the increase in fragility and hence in hæmolysis with time, the values being ex-

TABLE II.

Days storage	*300*	*100 (isotonic)*	*Percentage of hæmolysis in buffered saline solutions* (Simmel's) *90*	*80*	*70*	*60*	*55*	*45*	*40*	*0 (H_2O)*
1		0	0	0	0	2	4	14	87	100
2		0	0	0	0	4	10	33	87	100
3		0	0	1	5	11	11	77	..	100
4		2	..	5	9	17	39	85	..	100
8		2	2	5	19	34	60	97	100	100
10		5	5	24	35	60	84	94	100	100
15		10	31	64	67	86	96	..	100	100
22		..	61	85	87	94	94	94	100	100
35		59	79	87	85	97	..	..	100	100
50	12	75	..	..	95	..	..	..	100	100

Blood-citrate (1:1/5) rotated at 3° C.

pressed as percentage of the total hæmoglobin in the original sample.

The rate of increase in fragility with time is slower, the higher the concentration of the test solution. The presence of glucose in preservative solutions greatly improves stability.

As the volume of the corpuscle increases during storage, less additional swelling is required to cause hæmolysis. As shown in the previous table, the saline concentration at which hæmolysis begins gradually shifts towards "isotonic" and then into the normally hypertonic range. For purpose of discussion it is convenient to refer to the lowest concentration of saline that prevents additional hæmolysis, as the "critical saline concentration". The latter, therefore, is the concentration which is isotonic with the contents of the corpuscle at any given time, or, more strictly speaking, the concentration which is isotonic with the most fragile cells. As time goes on the critical concentration increases, and after a few weeks' storage may reach 2 or 3 per cent. The critical concentration will presumably be slightly hypertonic to the less fragile cells, and will be isotonic with plasma at the time. In the Table the values represent the total hæmolysis, that is, the degree of hæmolysis in the sample at the time, plus additional hæmolysis that may be caused by the test solution.

To ascertain the degree of spontaneous hæmolysis it is necessary to resuspend the corpuscles and either allow them to settle again or accelerate the process by centrifugation. The latter treatment invariably causes further cell breakdown. Spontaneous sedimentation, on the contrary, particularly in samples a few weeks old, is too slow to be practicable. One way of surmounting these difficulties is to do a fragility test on the suspended sample, using saline above the critical concentration. The free hæmoglobin in the supernatant solution may be estimated in the usual way, or, if concentration is very low, by means of the micro-chemical method of Wu[29] or of Barrett.[34]

As soon as preserved corpuscles show a tendency to hæmolyze in normal saline they will also break down, though to a smaller extent, in compatible plasma or serum. Presumably, also, they would undergo a similar destruction if transfused. Testing stored samples against fresh plasma or serum, therefore, gives an indication of their suitability for clinical use. Stored plasma or serum originally prepared from fresh blood is as good as fresh material for such tests.

In performing cell counts on stored specimens, Maizels[2] has recommended the use of plasma in place of normal saline, as diluent. As pointed out previously, however, some hæmolysis may occur even in fresh plasma or serum. If the actual number of intact cells in the sample is to be determined, therefore, it is necessary to use a hypertonic diluent above the critical concentration.

TABLE III.

Sample	Days storage	Total Hgb. grams percentage	Percentage hæmolysis in saline solutions								Percentage hæmolysis based on free Hgb. in plasma
			0 (water)	70	80	90	100 (isotonic)	200	300	400	
$15A_1$*	72	9.7	100	91	85	74	33	16	14	10	12.5
$18A_1$	41	10.4	100	73	53	42	12	12	8	8	8.6
$19A_1$	33	10.0	100	58	42	30	5	5	4	3	5.0
$22A_1$	21	8.8	100	35	19	9	3	3	2	0	2.3
$23A_1$	7	8.0	100	10	5	4	3	0	0	0	2.5

*A_1 = 1:1/2 dilution with citrate-glucose.

Table III illustrates the increase in fragility to hypertonic saline with time. Comparing the degree of hæmolysis in the various solutions with that estimated on the plasma, *i.e.*, spontaneous hæmolysis, it will be observed that solutions 200 and 300 produce almost no additional cell breakdown.

Influence of dilution on fragility of the cells.—The influence of dilution on the stability of corpuscles does not appear to be widely appreciated, and relatively few workers have given this matter systematic study. Table IV illustrates the effect of different dilutions on the stability of corpuscles to normal saline and plasma on the sixtieth day of storage. All samples are from the same blood specimen.

In the above series isotonic citrate (3.2 per cent solution of the dihydrate) and isotonic

glucose (5.4 per cent solution) were used as preservative. The degree of hæmolysis, estimated on the plasma, is expressed in per cent of the total hæmoglobin in the sample. It therefore represents the percentage of red cells broken down.

It is noteworthy in the above and similar series that the omission of glucose from the preservative always results in earlier and increased breakdown of cells. Optimal stability is usually obtained with a 1:1/2 dilution, but in the occasional blood a 1:1 dilution gives as good preservation. In the above series, however, the latter dilution is definitely inferior. The 1:1½ dilution usually gives excellent preservation in the refrigerator, but almost invariably the corpuscles undergo extensive hæmolysis when in isotonic saline or in plasma of the same blood group. The extent of

TABLE IV.

Sample	*Dilution*	*Percentage hæmolysis by supernatant plasma*	*Additional hæmolysis in isotonic saline*	*Additional hæmolysis in fresh plasma*
*14A_o	1:0.2	15	28	2
14A_1	1:0.5	4	14	1
14A_2	1:1	6	54	30
14A_3	1:1.5	4	81	39
14A_4	1:2	10	90	4

*Samples after 60 days' storage.

Key:

	Blood	*Citrate*	*Glucose*
A_o	5	1	0
A_1	5	1	1.5
A_2	5	1	4
A_3	5	1	6.5
A_4	5	1	9

hæmolysis varies considerably with different blood specimens, but this dilution always favours fragility. A few additional examples are given in Table V.

The 1:2 dilution also often behaves in a curious manner. During storage the cells of this dilution generally break down more rapidly than those of the 1:1½ dilution but occasionally are more stable to normal saline and plasma. Why this improvement should be brought about by the higher dilution is difficult to explain. This improvement is not always seen; in fact, blood behaves erratically in these higher dilutions.

Blood specimen number 12 (Table V) was extremely unstable from the start. It was unique among all the specimens tested in this study in that the plain citrated sample without glucose, was the most stable of the series. The 1:1 and 1:1½ dilutions broke down completely when mixed with normal saline or plasma. In the 1:1½ dilution the cells usually show a marked instability towards normal saline immediately the sample is taken. During the succeeding few hours osmotic readjustments occur which result in somewhat increased stability for a few days, after which the fragility increases fairly rapidly.

The preservative influence of sugar.—It is now generally agreed that the presence of glucose in preservative solutions is beneficial to stability of the corpuscles. Few workers have given this matter systematic study and those who have, do not agree. Thus, Dubash and coworkers[1] recommend a concentration from 0.25 to 1.0 per cent, Bushby and associates,[11] 0.25 to 0.5 per cent, and De Gowin[35] favours a final concentration of about 3 per cent.

Experiments with different concentrations of glucose in the present investigation have led to the conclusion that the degree to which blood is diluted and the concentration of the diluting solutions are more important than the actual concentration of glucose in the final mixture. It has been found, as expected, that dilution with hypotonic solutions increases fragility and that the use of isotonic or slightly hypertonic diluents increases stability of the corpuscles. Strongly hypertonic solutions are undesirable, since the corpuscles when mixed with plasma or serum take up water and burst. After much experimentation, the mixture: blood-citrate-glucose in the proportion 5:1:1.5 previously described (page 452), was found to give the most satisfactory preservation.

This gives a 1:½ or 2:1 dilution with isotonic diluent and a final glucose concentration of 1.08 per cent. Maintaining the above proportions and increasing the glucose concentration by adding hypertonic glucose had an adverse effect. Unfavourable results were obtained also by lowering the sugar concentration by adding less isotonic glucose, incidentally, changing the proportion of blood to diluent. It is obviously impossible to lower the glucose concentration and retain the above proportion and isotonicity. It was apparent from many experiments along this line that the degree of dilution and the use of isotonic diluent were more important factors than the final concentration of sugar in maintaining the red cell.

TABLE V.

INFLUENCE OF DILUTION ON STABILITY OF CORPUSCLES

Sample	Blood Diluent	Percentage hæmolysis in isotonic test solution after the following periods of storage																						
		0	1	2	5	6	7	9	10	12	14	16	22	24	26	28	31	32	33	34	42	44	56	62	80 days
$12A_0$	1:1/5	0			0							2											70		
A_1	1:1/2	17			16							18											85		
A_2	1:1	100			100							85											91		
A_3	1:1½	100			100							55											94		
$13A_0$	1:1/5		0	0												..									..
A_1	1:1/2		0	2												5									..
A_2	1:1		0	0												4									14
A_3	1:1½		0	2												5									28
$15A_0$	1:1/5		0			1.5			4	5.6								18						41	
A_1	1:1/2		0			0			1.7	1.8								8.5						34	
A_2	1:1		0			4.2			2.3	4.2								55						..	
A_3	1:1½		3			5.5			33	41								99						..	
$17A_2$	1:1		0					4.5		2.3	0		0						4.4			4.4			
$18A_0$	1:1/5	0	0				0								..		25		19		..				
A_1	1:1/2	3	0				0								0		0		0		4.8				
A_2	1:1	7	0				0								0		0		14		13				
A_3	1:1½	10	0				42								31		46		46		48				
$19A_1$	1:1/2	..		0		0							?	0						2					
$22A_1$	1:1/2		0			0		0		2		2	2												
$23A_1$	1:1/2									3							7.5				6.5		14		
A_3	1:1½									4							34				64		75		
$24A_1$	1:1/2										0			3					8						
A_3	1:1½										52			66					84						
$25A_1$	1:1/2														4			5		3					
A_3	1:1½														33			60		72					

Key to dilutions:

Samples:	Blood	Isotonic citrate (3.2%)	Isotonic Glucose (5.4%)
A_0	5 parts	1 part	0 parts
A_1	5 "	1 "	1.5 "
A_2	5 "	1 "	4.5 "
A_3	5 "	1 "	6.5 "

In the earlier part of this investigation the protective influence of common sugars including glucose, fructose, mannose, sucrose, maltose and lactose, and of polysaccharides, such as glycogen, starch and dextrin, was studied. All have a stabilizing influence on the red cell, but the order of merit varies with different bloods. In a few instances fructose and sucrose gave better preservation than glucose, but not in marked degree. Sucrose apparently remains unchanged during storage, but in its presence glycolysis of the blood glucose is somewhat more rapid. Ordinarily, at low temperature (4° C.) the glucose falls rapidly to about 14 mg. per cent, and then gradually to zero after several days. Sucrose itself remains unchanged for weeks, as may be demonstrated by means of invertase (see Table VI). Sucrose, therefore, does not give rise to lactic acid during storage, hence does not influence the pH of the sample. The main objection to sucrose is that when given intravenously it is non-utilizable and is quantitatively excreted into the urine, sometimes causing kidney damage. It will be observed that in the presence of an excess of glucose, glycolysis proceeds less rapidly than at the normal blood concentration.

It would appear that the addition of a polysaccharide such as glycogen or starch might assist preservation of corpuscles in two ways. First, a fairly constant glucose level might be maintained by the action of blood diastase, and, secondly, the polysaccharide being a colloid, might offset to some extent the colloid osmotic pressure within the cell, and thereby reduce the rate of swelling. That these substances do maintain the sugar level in blood during storage is

shown in Table VI. Glycogen is more rapidly hydrolyzed than the others and the enzymatic activity apparently diminishes after about the tenth day. The breakdown of starch and dextrin, on the other hand, proceeds at a more uniform rate.

TABLE VI.
SUGAR VALUES ON STORED SAMPLES

Days	No added sugar	Carbohydrate added				
		Glucose	Glycogen	Dextrin	Starch	Sucrose
0	83		83	83	83	83
1	47				58	
2	27	497		83		
3					58	14
4	14					
5	trace					0
6	trace					
7		484			67	
8	0					
10		428				
11			149	79		
12					63	
14			120	58		0
18		428				
20			104			
25		412				
28			92			
29						224 after invertase
34				39	65	

The effect of polysaccharides on the red cells is always beneficial but variable. One objection to their use is the resulting increase in viscosity of the samples and the difficulty in resuspending the corpuscles homogeneously without prolonged agitation. Furthermore, filtration of such samples is difficult. These drawbacks were overcome by storing blood in vessels coated on the inside with a layer of starch or dextrin jell. By so doing, glucose was maintained at a still higher level and preservation was good, but variable. The extra work involved in preparing containers, however, outweighs any merits of the procedure.

Gelatin and various gums added to citrate-glucose preservative or coated on the walls of the containers exhibited no special merit. Glycerol has an adverse influence on the stability of corpuscles. Numerous experiments were performed in which citrated blood was stored in dialyzing sacs of Visking sausage-casing surrounded with a jelled mixture of gelatin, citrate and glucose, or of dextrin containing citrate and amylase. In some instances the outer solution was changed periodically. In this way it was anticipated that the removal of lactic acid and other diffusible autolytic products might be beneficial. The behaviour of the samples was interesting, particularly regarding the shift of water, but it was impossible to tell what was happening. Preservation under these conditions was not superior to that obtained in the ordinary way.

Distribution of electrolytes in preserved blood. At the outset of this study an effort was made to correlate fragility with disturbance of the electrolyte balance of the corpuscles. Blood was stored in small tubes at 4° C. and at room temperature. It was anticipated that at the latter temperature similar but much more rapid changes would occur, thus making possible a speeding-up of storage experiments. At both temperatures some of the samples were kept stationary, while others were placed on a rotating shaft driven at a uniform rate of one rotation an hour by means of an electric clock. By this means the tubes were rotated about their horizontal axis and the corpuscles were maintained in loose suspension with a minimum of mechanical agitation. At suitable intervals tubes were removed for potassium, sodium and chloride analysis.

Potassium begins to escape from the cells almost immediately blood is drawn and at a rate which remains almost constant for about ten days. The rate may vary with different bloods and is influenced by the nature of the preservative and the degree of dilution. Although diffusion of ions is less rapid at lower temperatures, the loss of potassium from the cell is actually more rapid at 4° C., which indicates that the cell membrane is more permeable to this ion at the lower temperature. From about the tenth day the rate of diffusion diminishes when the plasma potassium reaches about 125 mg. per cent. Because of continual hæmolysis an equilibrium between cells and plasma is never reached; hence the curve continues to rise for several months until almost all the corpuscles have broken down. Under the conditions of storage used in the present investigation the plasma potassium and other values invariably fluctuate after about the fourteenth day of storage. The potassium may rise only slightly but more frequently falls. In the majority of instances this change occurs about the twentieth day. The twenty-eighth day usually initiates another change marked by a rise in plasma potassium. This occurs repeatedly when blood is stored in narrow containers and is seen even when samples are rotated.

During the initial period of storage cell potassium and plasma sodium tend to exchange places, but diffusion of potassium is favoured by greater permeability of the membrane to this ion and by its greater mobility due to its lesser degree of hydration. If permeability were not influenced by dilution it would be expected that the latter should favour increase in plasma potassium and decrease the rate of fall in plasma sodium, particularly in undisturbed samples. Storing cells in the suspended state favours uniform change, whereas in the superiority over the least favourable (blood-citrate 1:1/5) is not considerable.

The influence of lithium on fragility and on the diffusion of potassium and sodium was studied in several experiments. Lithium citrate (2.7 per cent) was used in place of sodium citrate in the regular preservative mixture. Its influence on fragility varied in different bloods, but in the majority of cases was practically the same as with sodium citrate up to about the twenty-seventh day, after which, almost invariably, the fragility increased

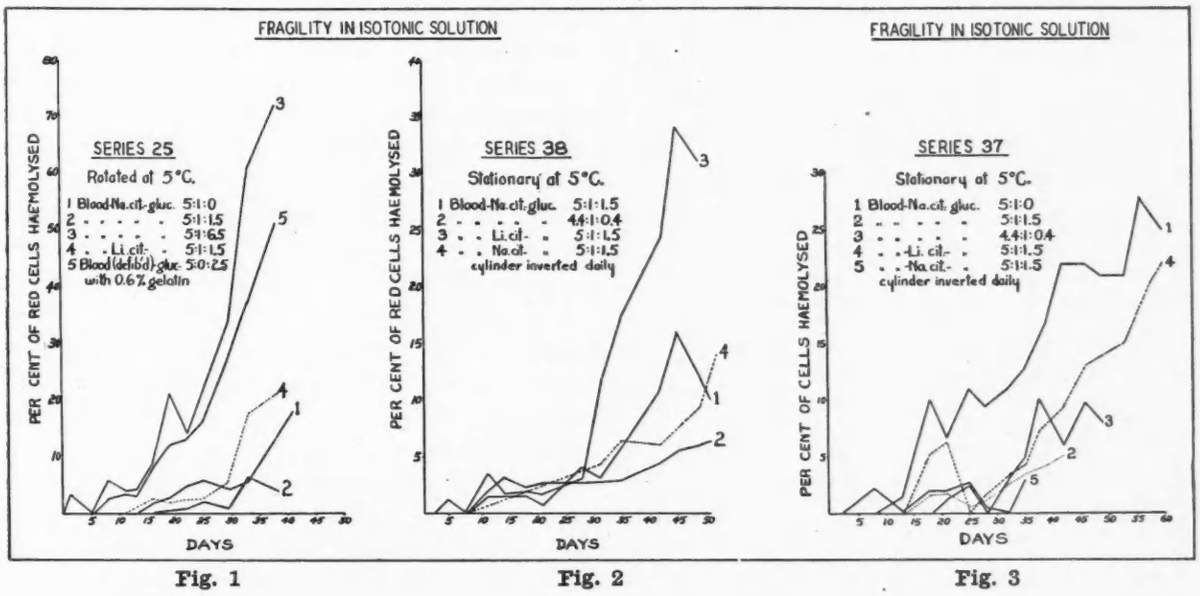
FRAGILITY IN ISOTONIC SOLUTION
SERIES 25
Rotated at 5°C.
1 Blood-Na.cit.-gluc. 5:1:0
2 . . . . . 5:1:1.5
3 . . . . . 5:1:6.5
4 . . Li.cit- . 5:1:1.5
5 Blood (defib'd)-gluc. 5:0:2.5
with 0.6% gelatin
PER CENT OF RED CELLS HAEMOLYSED
DAYS
FRAGILITY IN ISOTONIC SOLUTION
SERIES 38
Stationary at 5°C.
1 Blood-Na.cit.-gluc. 5:1:1.5
2 . . . . . 4.4:1:0.4
3 . . Li.cit- . 5:1:1.5
4 . . Na.cit- . 5:1:1.5
cylinder inverted daily
PER CENT OF RED CELLS HAEMOLYSED
DAYS
FRAGILITY IN ISOTONIC SOLUTION
SERIES 37
Stationary at 5°C.
1 Blood-Na.cit.-gluc. 5:1:0
2 . . . . . 5:1:1.5
3 . . . . . 4.4:1:0.4
4 . . Li.cit- . 5:1:1.5
5 . . Na.cit- . 5:1:1.5
cylinder inverted daily
PER CENT OF CELLS HAEMOLYSED
DAYS

Fig. 1 **Fig. 2** **Fig. 3**

packed condition each cell may have a slightly different environment of electrolyte. As might be expected, the plasma potassium in rotated samples reaches a higher concentration before the curve begins to level off than in stationary storage. A comparison of the rate of increase in potassium with the increase in cell fragility shows no relationship between the two processes. Potassium rises rapidly regardless of conditions of storage, whereas the stability of the corpuscle is greatly influenced by these factors. Plasma potassium, therefore, is not a useful criterion of the condition of stored blood.

To compare the influence of various dilutions on the shift of electrolyte it is necessary to calculate values back to a common dilution, *e.g.*, undiluted blood. This treatment is not strictly valid since it disregards other important factors. Considering the rate of escape of potassium in the most favourable dilution, *i.e.*, the most effective in retarding diffusion (usually 1:1) its rapidly. Typical fragility curves are illustrated in Figs. 1, 2 and 3.

In view of the extensive changes in distribution of potassium and sodium during storage a disturbance in chloride might also be expected. Analyses, however, show that plasma chloride remains remarkably steady. Slight fluctuations were observed from day to day which at first were attributed to experimental error but later were found to be due to variation in the degree of oxygenation of hæmoglobin. Because of difference in the air-space in different tubes the red cells are not oxygenated to the same degree in all samples when resuspended. The constancy of plasma chloride is shown in Table VII.

From the circumstance that the shift of chloride from the corpuscle during oxygenation is determined largely by the electrolytic dissociation of hæmoglobin, it might be anticipated that deterioration of the latter during storage should be reflected in a change in

TABLE VII.

PLASMA CHLORIDE (MG. %) DURING STORAGE

	Days									
Sample	*1*	*2*	*4*	*7*	*11*	*12*	*18*	*27*	*28*	*59*
$16A_1$		368	368	368	368		362		368	368
$16A_2$		380	374	374	368		362		351	374
$16A_3$			380	368	345		357		380	374
$16A_4$		351	351	328	328		345		345	351
$22A_1$	450	456	450			456		450		
$22A_2$	386	392	392			386		386		
$22A_3$	386	380	380			380		374		

chloride shift on oxygenation. So far data are available on only one long term experiment and are incomplete. As presented in Table VIII, however, they illustrate the behaviour of chloride when samples are equilibrated with carbon dioxide, alveolar air, and oxygen.

TABLE VIII.

	Hæmolysis in sample using test solution 300	*Plasma chloride after equilibration with*		
Day of test		*Carbon dioxide*	*Alveolar air*	*Oxygen*
1st (fresh)	0	293	345	380
2nd	0	303	345	382
3rd	0	303	351	374
11th	0	293	345	363
41st	2	293	...	362

It is well known that the corpuscles on oxygenation lose chloride and decrease in volume. Hæmatocrit readings were obtained but are unreliable because of the hæmolysis which occurs on centrifugation in older specimens. From the above experiment the plasma chloride apparently remained steady in the series equilibrated with carbon dioxide and alveolar air, respectively, but fell significantly in the fully oxygenated series with time of storage. A decrease in the range of shift might be due partly to the increasing amount of free hæmoglobin in the plasma, but there is no parallelism between the degree of hæmolysis and chloride transfer. The change in ionic composition within the cell might also influence ionization of oxyhæmoglobin. From evidence submitted in the following section it is unlikely that hæmoglobin undergoes deterioration in oxygen-carrying capacity within the forty-one day period of the above experiment. More definite interpretation of the behaviour cannot be made until extended experiments have been completed. The influence of differences in degree of oxygenation on plasma chloride, however, is apparent.

In experiments on preserved blood investigating the influence of oxygenation on potassium and sodium distribution, no change was observed.

Hæmoglobin.—A comparison of the rate at which darkening in colour of the corpuscles occurs at the beginning of storage and the rate of exchange of potassium and sodium between the cells and plasma at that time, strongly suggests a relationship between the two phenomena. From what is known about the influence of various ions on the properties of hæmoglobin,[25, 26] the above inference also fits in very well with the observed diminution in rate of oxygenation of red cells after several weeks' storage. Other possible contributory factors have been mentioned in an earlier section.

To ascertain whether the oxygen-carrying capacity of hæmoglobin decreases during storage oxygen determinations were carried out by the Van Slyke method, and the calculated hæmoglobin values were compared with those obtained with the photo-electric colorimeter. The results on these bloods are given in Table IX. These three specimens, preserved with citrate alone, were chosen because they represent the least favourable conditions of storage.

TABLE IX.

Sample	*Date collected*	*Date examined*	*G. percentage Hgb. by Van Slyke*	*G. percentage Hgb. by colorimeter*
$9A_0$	Feb. 6/40	Feb. 6		14.6
		May 3		14.7
		June 28	15.1	14.7
		July 22	14.2	13.2
$9B_0$	Feb. 6/40	Feb. 6		14.5
		May 9	15.3	
			17.2	
		July 23	16.5	14.9
				15.4
$15A_0$	Apr. 30/40	Apr. 30	13.7	12.1
		May 10	13.8	12.3
		July 23	14.6	12.6

It will be observed that the hæmoglobin values, both by the Van Slyke and colorimetric methods, remain very constant for months, and, apparently, may increase slightly with time of storage. The discrepancy in the values obtained by the two methods is probably attributable to a slight error in the constant used in making calcula-

tions in the colorimetric method. The higher values underlined were obtained when the samples were oxygenated for an hour or more. Care was taken to minimize loss of water by evaporation during aeration. This increase above the original value was frequently observed in older samples. The lowest pH found was 7.1. It appears, therefore, that hæmoglobin in blood stored at 4° C. retains its normal oxygen-carrying capacity for many months beyond the useful storage period. Furthermore, the use of the ordinary Evelyn colorimetric method for estimating hæmoglobin in samples preserved for long periods at low temperatures is valid.

At higher temperatures of storage, hæmoglobin is slowly converted to methæmoglobin. Several days at room temperature are required before methæmoglobin becomes detectable spectroscopically, but at 40° the change is rapid.

Although the hæmoglobin in samples at low temperatures retains its normal oxygen-carrying capacity for many months, the diminution in the chloride shift may possibly indicate a slight change in the degree of ionization of hæmoglobin on oxygenation. After several weeks' storage, there is a slight but noticeable sluggishness in the oxygenation process. It is possible that the hæmoglobin itself is not altered but that the increased sodium and decreased potassium in the corpuscle may influence the rate of oxygenation. The observed retardation may be explained also by the circumstance that during storage the hæmoglobin is practically depleted of oxygen, whereas normal venous blood contains a large proportion of oxyhæmoglobin. It is to be expected, therefore, that stored samples should require a longer time for complete oxygenation. These points are at present being studied further.

The darkening of colour in stored samples can be prevented by allowing ample air space in the samples and by inverting the container once a day to keep the corpuscles in suspension. These specimens remain bright red for months. The slight agitation given does not damage the cells, nor does storage in the oxygenated state increase fragility. Diffusion of potassium and sodium, however, is facilitated.

Other conditions of storage.—From experiments in which blood was stored under carbon dioxide, oxygen, air, nitrogen and hydrogen, the order of merit on the basis of freedom from spontaneous hæmolysis appeared to be in the order given above. In some cases the gases were bubbled through the samples in Nesbitt absorption flasks for a few minutes, and the pressure was brought to atmospheric pressure after cooling had taken place in the refrigerator. In other instances air simply was replaced by another gas. The bubbled samples all showed more rapid fibrin formation and hæmolysis.

In our experience, blood, however long preserved, remains odourless.

Storing blood in completely filled containers gives slightly improved preservation from the standpoint of appearance, but is not practicable because of the inconvenience and danger of contamination when the cells are to be resuspended.

An excellent statistical evaluation of the influence of various factors on the preservation of the corpuscle has been completed recently by Cook and associates.[71]

DISCUSSION

The storage of blood and its usefulness depend chiefly on three factors: (1) Stability of the corpuscle, *i.e.*, the cell membrane; (2) Stability of hæmoglobin, and (3) The absence of toxicity or other factors that may cause reactions on transfusion. The second of these requires no discussion since, as already indicated, hæmoglobin is one of the more stable constituents of blood, and undergoes no deterioration within the period of storage feasible at the present time.

The problem of reactions is a very important one, but is not peculiar to the use of stored blood. De Gowin and associates, and others, have shown that the incidence of reactions from blood stored up to ten or fourteen days is no greater than from fresh blood. Refrigerated samples up to forty-five days old have been used without reactions. From an analysis of the results of hundreds of transfusions, however, they observe that the frequency of reactions increases with time after the tenth day of storage. While the majority of reactions are mild, it is important, nevertheless, to ascertain their cause.

Some authors[36, 37] have stressed the elevated plasma potassium in stored blood as a possible cause of reactions. This apprehension, however, has been dispelled during the past two years by the successful use of preserved blood in thousands of transfusions.[38, 39] It has been shown from animal experiments, further, that

the slow administration of potassium salts has little effect on the blood potassium, the excess of the ion being taken up rapidly by the tissues and released gradually into the blood again for excretion.[40] The increased plasma potassium in preserved samples, therefore, should tend to alkalize the recipient's urine. Many workers[39] administer alkali whenever possible as a precautionary measure prior to transfusion of stored blood and others[68, 69] strongly recommend alkalization of all patients before and after transfusion of fresh blood. In cases of disturbed potassium metabolism the use of preserved blood would be undesirable.

One factor observed early in the present study as being a likely cause of mild and obscure reactions is the presence in stored blood of white-cell residues and particles or masses of fibrin. Numerous workers[64, 65, 67, 69, 70] have commented on the precipitation of fibrin but some appear to disregard it. Fibrin may precipitate in the form of microscopic shreds and as a loose clot, usually in the upper zone of the sedimented red cells with tenuous filaments extending downwards. When the corpuscles are re-suspended the fibrin masses, along with the remains of the white-cell layer, are broken into small fragments. The majority of these can be removed with ordinary straining devices used in transfusion, but a considerable amount of the finer particles may pass through. To retain these, a material of closer mesh, for example, heavy weight Swiss bolting silk (12 or 13 XX) of 130 to 160 mesh to the inch, is required. To what extent the finer particles constitute a hazard is not known. It would appear from the extensive and successful use of stored blood without extra precautions that complete removal of the particles is not necessary.

Fibrin-formation takes place slowly during storage regardless of the anticoagulant used. Heparin is less effective than citrate or oxalate in retarding the process, and a combination of heparin and citrate is inferior to the latter alone. Other anticoagulants also are ineffective. Doubtless the disappearance of prothrombin during storage, as observed by numerous investigators,[41, 42, 72] is related to this problem. As a rule the rate of fibrin-formation decreases with increased dilution of the sample. Defibrination would appear to be a logical solution to the problem, but, as already pointed out, this treatment markedly increases the fragility of the corpuscles. These questions will be discussed more fully in a later report.

The limiting factor in the preservation of blood by refrigeration is the instability of the corpuscle, *i.e.*, the cell membrane. Little is known regarding the nature of the change that takes place in the membrane almost immediately blood is drawn. Temperature has a marked influence, but restoring the temperature to 37° C. does not restore the normal impermeability to sodium and potassium. Maizels and Paterson[43] have submitted evidence that stored cells on transfusion undergo a sort of reconstitution with restoration of their normal chemistry within twenty-four hours. This, however, requires confirmation.

The influence of dilution on osmotic fragility of the red cell has already been emphasized. An extensive comparison of preservative solutions recommended by various workers has shown that dilution of blood with half a volume of isotonic diluent (citrate-glucose) gives optimal preservation in the majority of cases. Because of the differences in bloods there is no single solution that will give optimal results with all specimens. With many bloods the 1:1 dilution appears to be almost as satisfactory as the 1:½ dilution. We have found also that the 1:1/3 mixture used by Bushby and colleagues[11] is as good as the 1:½ during the first month. The latter dilution, however, appears to be generally the most satisfactory and tends to give a slower rate of fibrin precipitation than with smaller dilutions.

Larger dilutions, especially above 1:1, afford good preservation but tend to increase the fragility of cells to normal saline and to compatible plasma or serum. The instability to the latter is much less than to the saline but is considerable. Whether cells fragile to plasma at room temperature would break down if transfused has not been established, but is probable in view of the observations of Bushby and coworkers,[11] who followed the blood bilirubin after transfusion. It is noteworthy, however, that the Iowa group of investigators,[38] who have had very extensive experience in the use of stored blood, have used the 1:1½ dilution in hundreds of transfusions with complete success. Even if this dilution should increase fragility and give rise to some hæmolysis *in vivo*, about 80 per cent of the red cells in a 500 c.c. transfusion would

have to break down before the free hæmoglobin in circulation would exceed the renal threshold. This degree of destruction is extremely unlikely.

In the operation of many blood banks the redness of the plasma layer is still used as the criterion for judging the condition of samples. From what has been said previously it is apparent that the appearance of a sample in the refrigerator has little significance. In the present investigation the behaviour of samples toward fresh or stored plasma or serum (compatible) has been used for judging preservation. In the majority of cases 2.5 per cent saline gives fairly comparable results and eliminates the factor of compatibility. Tests of this kind make possible the detection of extreme fragility in specimens such as No. 12 (Table V) which appear to be quite well preserved, but may break down extensively on transfusion.

Opinions differ regarding the length of the safe and useful period of storage, but it is now quite generally accepted at least that blood stored up to 10 days is as efficacious as fresh blood. Some authorities[44] take this as the limit of useful storage, others 14 days,[45,46] and some 18 days[47] or even more.[11,39,48] The Bureau of Health of New York City has tentatively adopted the 18-day limit.[49] It has been demonstrated repeatedly, however, that blood stored for much longer periods can be used with good results. De Gowin and Hardin[39] consider five days to be the safe limit in the case of citrated blood, but have used samples stored for over thirty days by their method, with beneficial results. Schaefer and Wiener,[50] using Ashby's technique[51] of transfusing Group 0 cells into an A or B recipient and following the proportion of non-agglutinable cells (0) in the recipient, observed that blood stored up to eight days survived as long as fresh blood, *i.e.*, three to four months. Blood stored from ten to twenty days was found to survive from one to three weeks. Other investigators,[43,47,52] using the "M and N" method,[53] in which blood of group 0 type M is transfused into a recipient of group 0 type N, and the survival of the M cells followed by their agglutinability with rabbit immune serum (anti-M), have shown that there is scarcely any difference in survival of fresh and fourteen-day-old blood. In the case of the latter about one-third of the transfused cells remained on the seventieth day.[47] It is possible that further improvements in methods of preservation may extend the useful period of storage.

SUMMARY

Among the factors that have a marked influence on the stability of the corpuscle during storage are the concentration of the diluent or preservative, and the degree to which blood is diluted. Optimal preservation is obtained with an isotonic citrate-glucose diluent using one volume of blood to one-half of diluent as follows:

Blood: 5 parts.
Isotonic (3.2 per cent) sodium citrate: 1 part.
Isotonic (5.4 per cent) glucose: 1.5 parts.

Good preservation is usually obtained over a range of dilutions, namely between 1:¼ and 1:1, but the 1:½ mixture has been found most satisfactory for bloods in general. Blood diluted with more than an equal volume of citrate-glucose undergoes no more hæmolysis during storage than in lower dilutions, but is much more fragile to normal saline or fresh plasma. Since it is impossible to tell from the appearance of stored specimens how stable or fragile the corpuscles are, it is recommended that samples be tested against compatible plasma or a suitable hypertonic saline solution. This, at least will give some information as to how the corpuscles would behave on transfusion.

The oxygen-carrying capacity of hæmoglobin remains unchanged during the period of storage feasible on the basis of survival of corpuscles.

We are grateful to the National Research Council of Canada for financial assistance in this investigation, and to Professor J. B. Collip under whose direction the work was carried on.

With a few exceptions the blood used in this study was contributed by members of the Montreal Voluntary Transfusion Service. We gratefully acknowledge the willing co-operation of this organization and particularly of those members who donated blood. We appreciate also the assistance of the Child Welfare Association of Montreal in arranging for donations.

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A full bibliography can be found in the reprints of this article.

PEPTIC ULCER IN CHILDREN

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PEPTIC ulcer in children has been considered a rare condition, as only 36 cases have been reported.[1] Clinically and pathologically, peptic ulcers must be differentiated from other types of gastric ulceration common to childhood, such as those accompanying burns, malnutrition, melæna neonatorum, and acute infections such as meningitis, septicæmia, scarlet fever, etc. Post-mortem data of the incidence of gastric ulceration in children are not concerned usually with peptic ulcer but these other various types. This report deals with cases which pathologically and at times clinically resemble those found in adults.

The condition must be more prevalent than is realized. In nearly 10,000 cases of gastric and duodenal ulcers reviewed from the records of the Mayo Clinic, Proctor[2] found that there were only 3 children. But in 1,000 cases of gastric ulcer and 1,000 cases of duodenal ulcer he found that in 16 cases of gastric ulcer and 26 of duodenal ulcer the symptoms had been present since childhood. This is a collective incidence of 2 per cent, and it suggests that the diagnosis in many cases of children is being overlooked. Our own hospital records verify this conclusion. Prior to January, 1939, the youngest patient with peptic ulcer on record at the hospital and out-patient department was 17 years of age. All 8 cases presented in this article have been discovered since that date, probably not because the condition is more prevalent now, but because we have been searching for it.

Clinical diagnosis is difficult. This is especially true of cases under the age of ten years. Kennedy[3] states, "The signs and symptoms which are present may be few or many but are so diversified as to rob them of pathognomonic significance." I have found this statement to be uniformly true. Confusion is added by the fact that children under ten years of age are inaccurate in describing and localizing pain, and in designating areas of tenderness to the physician. They are particularly susceptible to suggestion, and for that reason should be asked no "leading" questions unless it is unavoidable.

The following series is composed of 8 children whose ages ranged from 6 to 14 years. There are 2 girls and 6 boys in the group. All ulcers were duodenal, except one (Case 3).

CASE 1

A male, aged 9, entered the hospital in November, 1939, with a tentative diagnosis of appendicitis. He had developed abdominal pain twenty-four hours before admission, which he described as a steady ache centered persistently around and above the umbilicus. He became nauseated and vomited once on the day of admission. During the three preceding years he had had several similar attacks, but none so severe as the present one. Between attacks he was free of abdominal discomfort.

Past history.—He had had varicella in 1933 and scarlet fever in 1935. The *family history* was irrelevant.

Physical examination.—He was a pale and poorly-nourished lad. The oral temperature was 101.2°. The tonsils were large but not inflamed or scarred. There was diffuse abdominal tenderness, more marked in the area of the umbilicus and right iliac fossa, but no rigidity. The rectal examination was negative. By the following morning tenderness could be elicited only in the epigastrium. The temperature was now normal.

Laboratory.—The urinalysis was negative. The white blood count was 4,150; the erythrocytes numbered 5,110,000, and the hgb. was 92 per cent. The sedimentation rate was 10 mm. in one hour. X-ray examination of the chest was negative. In the gastric analysis there was a free HCl of 17, total acidity of 50, and no occult blood.

For the next forty-eight hours, in spite of a soft diet, he consistently complained of nausea following meals. The stool contained occult blood (plus 2). Roentgenographic and fluoroscopic examination of the stomach and duodenum revealed an incisura and irregularity of the duodenal bulb characteristic of ulceration, but no definite crater. About one-fourth of the barium was retained in the stomach after five hours. He was placed on a modified Meulengracht diet.*

Within three days he was asymptomatic and the abdominal tenderness had disappeared. One month later there was only a trace of occult blood in the stools. He had gained three pounds and looked well. Immediately following discharge a second roentgenographic examination revealed a marked diminution of the irregularity, but there was still a five-hour retention of one-fourth of the barium meal.

Two months after discharge he again entered the hospital complaining of continuous epigastric pain of two days' duration. The complaints, physical, and x-ray findings were the same as for the first admission. He was again started on a modified Meulengracht diet with colloidal aluminum hydroxide every four hours. Improvement was distinctly slower. It was two weeks before the abdominal tenderness disappeared. At the present time he is asymptomatic, gaining weight, and looking well.

CASE 2

A male, aged 14, was sent into the emergency ward in September, 1939, with a diagnosis of appendicitis. For two and one-half months he had complained of intermittent abdominal pain occurring one to two hours before

* Graduated ulcer diet, giving a choice of plain, orange or citrated milk.

meals and relieved by food. Although he could not describe the pain, he located it in the epigastrium and left hypochondrium. He had vomited only once, a week before admission. His appetite was good.

Past history.—He had had mumps, varicella and pertussis but no recent illnesses. The father had a peptic ulcer. The mother and two sisters were well.

Physical examination.—The tonsils were greatly hypertrophied and scarred. Examination was otherwise negative.

Laboratory.—The urinalysis was negative. The white blood count was 6,350; the red blood count 4,710,000; and hgb. 84 per cent. The blood Kahn test was negative. The gastric analyses were unsuccessful. Roentgenographic and fluoroscopic examination revealed that the duodenal bulb filled poorly and was markedly irregular throughout the examination, strongly suggesting ulceration. There was no retention of barium in the stomach after five hours.

He was placed on a modified Meulengracht diet with an alkaline mixture mid-morning, afternoon, and at bedtime. Arrangements were made for him to have milk at school. Three months later he admitted that he had not adhered to the diet, but insisted he had had no return of the abdominal discomfort. There was no abdominal tenderness. In the stools, however, there was plus 3 occult blood. X-ray examination now revealed no evidence of ulceration, although the duodenal bulb was hard to fill. He is now continuing on the Meulengracht diet with colloidal aluminum hydroxide between meals and at bedtime.

CASE 3

A female, aged 11, entered the hospital on December 4, 1939, complaining of abdominal pain and fever of two days' duration. She described the pain as a dull constant ache centred around the umbilicus. There was no nausea or vomiting. For three months she had had several similar attacks and had also experienced mild discomfort at bedtime and before breakfast in the mornings. Throughout the day she was quite comfortable. This pain was not relieved by food.

Past history.—In 1935 she had had measles and an attack of rheumatic fever. She had a mild recurrent attack of rheumatic fever in 1936 but none since. Her father had died of pulmonary tuberculosis, and the mother had just been discharged from the hospital with an arrested pulmonary tuberculosis. Her Mantoux test (1:1,000) was strongly positive, but an x-ray examination of the chest was negative. Her mother stated she was exceedingly conscientious about her school work, studied hard, and worried a great deal about her lessons and her mother's health.

Physical examination.—She was well-developed but thin. The admission temperature was 102°. The tonsils were small but scarred. Examinations of the lungs and heart were negative. The abdomen was soft and there was only slight tenderness just around the umbilicus in the midline.

Laboratory.—The white blood count was 18,000. Polymorphonuclears numbered 81 per cent; lymphocytes 13 per cent; and monocytes 6 per cent. The red blood count was 5,070,000 and the hgb. 91 per cent. The sedimentation rate was 50 mm. in one hour. Two days later the temperature dropped to normal, the white blood count to 7,750, and the sedimentation rate to 20. There was plus 4 occult blood in the stools. In the gastric analysis there was a free HCl of 45, a total acidity of 64, and only a trace of blood. X-ray examination of the chest revealed only a few thickened nodules at both right and left hilus. Roentgenographic and fluoroscopic examination of the stomach and duodenum revealed a small filling defect on the lesser curvature of the stomach, suggesting ulceration.

She was started on a modified Meulengracht diet. Twenty-four hours later the abdominal discomfort and tenderness disappeared and she has been asymptomatic since. Two months after discharge from the hospital, the roentgenographic examination was repeated. The previously reported irregularity, though not so pronounced, was still present. Two months later no evidence of ulceration could be found. She is now on a general diet and symptomatically well.

CASE 4

A male, aged 12, entered the out-patient department in February, 1939, complaining of crampy intermittent abdominal pain over a period of two years. He definitely placed the position of the pain as mid-epigastric. Soda relieved the discomfort, but he had never tried food. The pain usually occurred at night. There was no associated nausea or vomiting, and there was no distress during the daytime.

Past-history.—He had had scarlet fever and pneumonia in 1931, and an appendectomy in 1934, following an attack of acute appendicitis. His tonsils had been removed in 1936. Because of the resemblance to a Fröhlich's type of obesity he had been started on thyroid extract at that time. The family history was irrelevant.

Physicial examination.—He was a fairly obese lad, weighing 105 pounds. Although the fat distribution was quite general, there was an accentuation in relation to the girdle area and breasts. The genitalia were infantile. Both testes were in the scrotum. There was no pubic or axillary hair. Mild epigastric tenderness could be elicited, but there were no other findings of importance.

Laboratory. — The stools were negative for occult blood and the urinalyses negative. The blood Kahn test was also negative. Roentgenographic examination showed evidence of duodenal ulceration at that time, and one month later a large ulcer crater was demonstrated in the duodenum. He was placed on a modified Meulengracht diet with magnesium trisilicate between meals and at bedtime. He become asymptomatic in two weeks and has been subjectively well since.

On re-examination in January, 1940, there was no abdominal tenderness. The blood findings were normal and there was still no occult blood in the stools. Roentgenographically, there was a "waist" involving the duodenum which remained throughout the examination. However, there was no residue in the stomach after five hours.

CASE 5

A male, aged 9, entered the outpatient department in December, 1939. For three months he had been losing weight and complained of being tired most of the day. His appetite was poor. For a year he had complained of intermittent pain in the knees and groins when walking, but during the previous three months they had occasionally been so painful as to wake him during the night. He had had innumerable colds and sore throats in the previous year. He also complained of vague abdominal cramps (no localization), constipation, frequency and dysuria, headaches, and blood in the stools. The last complaint had appeared only a week before admission. According to the mother the stools had been streaked with dark red blood but were not "tarry". He complained of some abdominal pain at night and sore stomach in the morning. He had suffered from enuresis since birth but the dysuria was a recent complaint.

Past history.—He had had pertussis as a baby and was told he had had rheumatic fever a year before. The attack was followed by pleurisy of short duration. The mother was well, but the father had a long history of undiagnosed "indigestion". A brother was in the hospital convalescing from a pneumococcic meningitis, and two sisters were at home, well.

Physical examination.—He was not so acutely ill as his history might signify. He was pale and undernourished. The tonsils were enlarged and scarred, and there was good evidence of recent infection. The cervical glands were hard and discrete but not tender. He had prominent glands in both axillæ and inguinal regions, the latter set very tender. The abdomen was diffusely tender, more pronounced in the epigastrium and both lower quadrants. There was no rigidity. He was distinctly tender in both knees and hip joints and along the distribution of the left sciatic nerve. There was no

swelling of the involved joints. Rectal examination was negative.

Laboratory.—The stools were negative for occult blood. The white blood count was 11,000. Polymorphonuclears numbered 61 per cent, lymphocytes 32 per cent, monocytes 1 per cent, and eosinophiles 1 per cent. The red blood count was 4,800,000, the hgb. 100 per cent and the sedimentation rate 45. Platelets numbered 120,000. The blood Kahn test was negative. The urine showed plus 3 albumin and plus 3 white blood cells. Roentgenographic and fluoroscopic examination of the stomach and duodenum revealed an irregularity of the duodenum, suggesting ulceration. X-ray examination of the chest was negative and the Mantoux test (1:1,000) gave no reaction.

He was admitted into the hospital in January, 1940, for further observation. By this time he was improving. His sedimentation rate was now 18, but the white blood count was still 11,000. He had no fever. The joints were distinctly less tender. The urine continued to show albumin and pus, but no red cells or casts. The non-protein nitrogen was 29 mg. An intravenous pyelogram was essentially negative. Culture of the urine showed colon bacilli and streptococci. He concentrated the urine well. He was placed on prontylin and a bland diet. Two weeks later he had no complaints, although there was still some tenderness in the epigastrium. His appetite improved remarkably. The urine continued to show various amounts of albumin, but this proved to be orthostatic. On February 6th roentgenographic examination revealed no evidence of lesion in the stomach or duodenum. His tonsils and adenoids were removed before discharge. At the present time he is on a slightly restricted diet. There has been no return of symptoms.

CASE 6

A male, aged 9, entered the outpatient department in February, 1939. His chief complaint was epigastric pain of six months' duration. He complained so much at night that his mother could not understand how he slept enough to keep awake the next day. In the mornings he always had a stomach ache. "He ate incessantly all day long to keep his stomach from aching." For three successive winters a diagnosis of rheumatic fever had been made because he was feverish at night, but there were no joint pains or chorea. He had lost weight, the exact amount of which was undisclosed.

Past history.—He had had varicella as an infant, and a tonsillectomy was performed in 1938. The *family history* was negative.

Physical examination.—He was a pale lad, weighing but 55 pounds. The temperature was normal. With the exception of slight abdominal tenderness in the area of the umbilicus there were no positive findings.

Laboratory.—The blood Kahn test was negative. The sedimentation rate was 10. The urinalysis was negative and the stools contained no occult blood. Roentgenographic examination of the stomach and duodenum revealed a marked irregularity of the duodenum, suggesting ulceration.

He was placed on a modified Meulengracht diet and sent to a convalescent home. After one week he had no further abdominal distress. He was called back to the clinic in January, 1940, for re-examination. He now weighed 64 pounds and was feeling well. Physical examination was entirely negative. The stools contained no occult blood. Roentgenographic examination revealed no evidence of a lesion in the stomach or duodenum.

CASE 7

A female, aged 7, entered the out-patient department in March, 1939. She had complained of epigastric pain of an intermittent type for eight months. The pain occurred during the day most commonly following meals, and at times she would complain of pain during the night and early in the morning before breakfast. Occasionally she would become nauseated and vomit. Vomiting would relieve the pain. Her mother thought she was often constipated. Her diet consisted largely of foods fried in olive oil and highly seasoned foods which the family relished.

Past history.—She had had varicella as a small child and a tonsillectomy in 1938. The family history was negative.

Physical examination. — She was a well-developed, well-nourished girl. There was a slight tenderness around the umbilicus but no rigidity. Examination was otherwise negative.

Laboratory.—The red blood count was 4,200,000 and the hgb. 74 per cent. The white blood count was 6,700 with 48 per cent polymorphonuclears and 52 per cent lymphocytes. The stools were not examined for occult blood. In the gastric analysis the free HCl was 30 and the total acidity 49. Roentgenographic examination of the stomach and duodenum revealed a slight amount of irregularity of the lesser curvature of the stomach near the cardia and some irregularity of the duodenum suggesting ulceration.

She was referred back to her physician for treatment, and was not seen again until January, 1940. She had been placed on a bland diet with Sippy powders between meals and at bedtime. Although she still had occasional attacks of abdominal pain they were much milder and farther apart. Examination of the blood and stools was now essentially negative. Roentgenographic examination revealed no evidence of irregularity of the stomach or duodenum.

CASE 8

A male, aged 11, was sent into the hospital on November 15, 1939, because of pallor and "tarry" stools. One year prior to admission he had complained of occasional abdominal pain following meals. Lying down seemed to relieve it. In the early part of January, 1938, he had had a severe attack of abdominal pain, necessitating a "hypo" for relief. Simultaneously the stools became almost black, although they returned to normal in two weeks' time. The pain also disappeared entirely, and within a month he was well. In September, one month before admission, the stools again became tarry and it was noticed he was very pale. No pain accompanied this attack. Two weeks before admission the stools again became black and the pallor very marked. He felt well, however, and had no complaints.

Past history.—He had had measles and a number of colds and sore throats, but none recently. The *family history* was negative.

Physical examination.—He was a pale and thin lad. The tonsils were large but not inflamed. He had two carious teeth. The tongue was heavily furred. No abdominal tenderness was present. The rectal and proctoscopic examinations were negative.

On the second day of admission he had gross but painless hæmaturia which continued for two days and then entirely disappeared. The tourniquet test was negative.

Laboratory.—The red blood count was 3,200,000 and the hgb. 56 per cent. The white blood count was 6,800, with 54 per cent polymorphonuclears, 5 per cent metamyelocytes, 38 per cent lymphocytes, 1 per cent monocytes, and 1 per cent eosinophiles. The sedimentation rate was 20. The stools were tarry and contained occult blood (plus 4). The platelets numbered 270,000. The bleeding and clotting time were normal. The non-protein nitrogen was 37 mg. In the gastric contents there was no free HCl, a total acidity of 17, and plus 3 and plus 4 occult blood in all specimens. An intravenous pyelogram was negative. Roentgenographic and fluoroscopic examination revealed the characteristic crater of an ulcer in the duodenum.

The lad was placed on a modified Meulengracht diet. He was asymptomatic during his entire hospital stay, although the stools continued to show plus 4 occult blood until one and one-half months later, when he was started on colloidal aluminum hydroxide every two hours. During this time he had been given five transfusions to offset the anæmia accompanying the continual loss of blood. Within a week after starting the colloidal aluminum hydroxide the occult blood in the stools dis-

appeared, and it did not rise above a trace until after discharge from the hospital. At the end of two months roentgenographic examination revealed no evidence of duodenal ulcer. The red blood count was 4,000,000 and the hgb. 84 per cent on discharge.

He had dark stools for several days following discharge, but at the present writing there is no melæna. He looks and feels well. Physical examination is completely negative. He is continuing on the prescribed diet with colloidal aluminum hydroxide between meals and at bedtime.

COMMENT

Attempts to determine etiological factors were very discouraging. Adult contributory causes such as alcohol, tobacco and emotional strain are almost negligible. Although infection was not a notable feature, nevertheless it is felt that all foci, either active or recently active, should be eradicated. The subject of dietary indiscretion cannot be properly evaluated; children are renowned for dietary imprudence.

It is significant that 6 of the 8 children were definitely under weight. All belonged to families of low income, most of them on relief. This in itself furnishes a good indication that the diets were deficient in certain essential foodstuffs, notably protein. It is estimated by our dietitians that the average relief diet contains about 65 per cent of the optimal protein requirements for a growing child. How much emphasis should be placed on this factor is not known. It has been shown recently that high protein diets can be used with a moderate degree of success in the treatment of peptic ulcer in adults.[4]

In 2 cases there was a significant family history. In Case 2 the father definitely had an ulcer, and in Case 5 the father gave a long history of indigestion, but was not under treatment.

No further stress need be placed on the diversity of symptoms. The single feature in the symptomatology is the duration of the abdominal pain. Individually, the span is from two and one-half months to three years, with a group average of one year. In patients 1, 2 and 3 the pain was so severe they had been sent to the hospital with diagnoses of acute appendicitis. Seven of the 8 localized the pain in the epigastric and paraumbilical region of the abdomen. In Cases 3, 4, 6 and 7, the pain appeared with noticeable regularity during the night and before breakfast in the morning. This would seem to parallel the pain of adults which occurs with greatest frequency after the stomach has emptied, except that in children the interval between food ingestion and the onset of the pain is greatly prolonged. Cases 2, 4 and 6, gave a definite history of relief from food or soda, and, as might be expected, the two oldest members of the group presented this phenomenon which is so characteristic in the adult. Nausea and vomiting occurred in only 3 cases, but in 2 of these it had occurred on only one occasion each. We feel that it is not important as an aid in the diagnosis of ulcer, but rather tends to confuse the diagnosis with other intra-abdominal conditions, such as appendicitis, for which an unnecessary operation may be performed. This is also true of fever, leukocytosis, and increased sedimentation rate which occurred in 2 cases each. In these instances they were thought to be due to an infection elsewhere that may have been the precipitating factor in re-activating an ulcer already present. Patient 1 narrowly escaped operation on the night of admission because of the history, nausea and vomiting, the fever, and the nature of the abdominal pain.

Loss of appetite was present in only 2 cases, and in Case 1 this amounted to a veritable sitophobia, the abdominal distress and nausea following the ingestion of food. Pyrosis, eructation and flatulence were notably absent in the histories. They may have been present but undisclosed because of the patient's inability to describe the symptom. Although constipation has been reported a common complaint, it occurred in only 2 cases in this group.

Abdominal tenderness was the most constant physical sign. It occurred in 6 cases and was more pronounced in the epigastrium and paraumbilical regions. In 2 patients there was a slight diffuse tenderness elsewhere; in 2 there was no abdominal tenderness at any time.

Anæmia was present in only one case, and this was due to an extensive loss of blood by the bowel previous to and following admission. Occult blood was present in the stools in 4 cases. The test, when done repeatedly, is an aid to diagnosis and a check on the efficacy of treatment. The results of gastric analyses were so inconclusive that they would seem to be of little practical value.

Because of the diversity of subjective and objective findings it is impossible to make more than a presumptive clinical diagnosis of ulcer, so that the burden must fall upon the roentgenologist. In one way this is unfortunate, because in most hospitals there is very little occasion to have gastro-intestinal series in children of this age. The natural conservatism of the roentgenologist makes him very hesitant in committing himself to the presence or absence

of a lesion in children, especially in cases where no crater is demonstrable. This need not be. Our knowledge in this matter has been gained not only by the advice of our roentgenologists but by the roentgenographic and fluoroscopic appearance of the stomach and duodenum in a number of control patients. Peristalsis seems to be normally more rapid in children. Otherwise, there is little essential difference in the roentgenographic appearance in children and adults. I stress this point because in only 3 of our cases were we able to demonstrate an actual crater. The remaining 5 cases were reported as having "a marked irritability and irregularity of the duodenum, suggesting ulceration". Such an interpretation does not necessarily connote that the ulcer is active, but when coupled with suggestive clinical findings we may well assume that it is. Proctor[2] states, "Even among roentgenologists of wide experience few will make a definite diagnosis of ulcer, but the fact that a lesion is present will usually be noted."

Two cases presented definite complications; one (Case 8) with a severe and rather persistent hæmorrhage which was manifest by tarry stools; the other (Case 4) with a moderate degree of stenosis revealed by x-ray but unaccompanied by untoward symptoms. There was retention of the barium meal in 3 cases when first seen. This disappeared with treatment in Cases 6 and 8, but was present in Case 1 following two months of diet alone.

Six patients were placed on a modified Meulengracht diet, and the other two on a bland diet that served the same purpose. In all but cases 7 and 8 the relief from symptoms was almost immediate. Three cases were placed on colloidal aluminum hydroxide; case 8, because of the persistence of duodenal hæmorrhage that did not respond to diet alone; cases 1 and 2, because of subsequent relapses. Patient 2 admittedly would not stay on his diet. Patient 7 has had mild recurrences of abdominal discomfort. Seven of the 8 cases are asymptomatic at the present time. The last roentgenographic examination on this group revealed no evidence of activity in 7 cases.

It is too early to properly evaluate the results of our treatment. As with other illnesses in children, the reparative processes seem to be great.

SUMMARY

In the child, as in the adults, the etiological factors of peptic ulcer are questionable. The clinical picture is variable. The one important complaint which should always arouse suspicion is the history of long-standing abdominal pain, recurrent or chronic. The older the child, the greater the tendency for the picture to resemble the adult symptomatology.

The most constant physical sign is abdominal tenderness, although it may be absent at the time of examination. It is usually epigastric or paraumbilical.

The diagnosis must depend upon the roentgenographic examination. Though desirable, the demonstration of a crater is not always possible or necessary. If a constant and characteristic deformity of the duodenum can be demonstrated roentgenographically in a child with sufficient clinical and laboratory evidence of ulceration, then the diagnosis of peptic ulcer is justifiable.

I wish to express appreciation to the Pædiatric Staff of the Vancouver General Hospital for their co-operation and suggestions, and especially to Drs. E. S. James, J. R. Davies, and E. J. Curtis for the use of their cases.

REFERENCES

1. KELLOGG, H. B.: Chronic peptic ulcers in children, *Northwest Med.*, 1939, **38**: 129.
2. PROCTOR, O. S.: Chronic peptic ulcer in children, *Surg., Gyn. & Obst.*, 1925, **41**: 63.
3. KENNEDY, R. L. J.: Peptic ulcer in children, *J. of Pediat.*, 1933, **2**: 641.
4. WINDER, C. AND MATZNER, M. J.: Peptic ulcer—The effect of high protein diet on the behaviour of the disease, *Am. J. of Digest. Dis.*, 1939, **5**: 743.

RÉSUMÉ

La littérature médicale ne révèle que 36 cas d'ulcère peptique rapportés chez les enfants. Cet état est probablement plus fréquent. Les circonstances étiologiques sont assez difficiles à établir et l'image clinique est très variable. Il semble que le symptôme le plus fidèle soit la douleur abdominale intermittente et récidivante. Chez le grand enfant les symptômes se rapprochent de plus en plus de ce que l'on observe chez l'adulte. Les malaises abdominaux ont cette caractéristique de siéger, soit à l'épigastre, soit au niveau de la région péri-ombilicale. Le diagnostic précis nous viendra de la radiographie de l'estomac et du duodénum. Les 8 cas rapportés soulignant l'importance de la douleur intermittente et du malaise récidivant.

JEAN SAUCIER

TUBERCULIN AS A THERAPEUTIC MEASURE IN OPHTHALMOLOGY*

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THIS paper is really an argument in favour of tuberculin. I am a firm believer in tuberculin therapy in ophthalmology because, first, many cases of eye disease are caused by tuberculous processes; secondly, properly executed tuberculin therapy does a great deal of good and no harm; and, thirdly, if it were not for tuberculin our treatment of these conditions would be very unsatisfactory. That there are tuberculous eye conditions is obvious—there can be no dispute about that. In 1926 Meller, of Vienna, said that tuberculosis is a more important cause of irido-cyclitis than is ordinarily thought. Also in 1926 Verheoff said that anterior nodular scleritis is always due to tuberculosis. Our feeling now is that, whereas tuberculosis is the commonest cause of scleritis, this condition can also be caused by rheumatism and foci of infection. At that time also it was computed that tuberculosis was the cause of 10 per cent of cases of uveitis in the United States, while in Germany it was computed as 50 per cent. The figure likely lies somewhere between these two. Wilmer[1] analyzed a group of cases and computed that 40 per cent of the cases of uveitis are due to tuberculosis. I am not one of those who want to blame tuberculosis always for these conditions. I am only glad if I can find other causes and treat them accordingly.

In relation to our second point that properly executed tuberculin therapy does a great deal of good and no harm, we have the results of clinical experience and the observations of such authorities as Wilmer, Knapp, Gifford and Gay. In Gay's excellent article[2] he gives the results of the treatment of 30 selected cases with seriously diseased eyes. In these the only thing found after extensive investigation was tuberculin hypersensitivity. No patient was made worse, and in the majority the result of the treatment was the restoration of an eye supposedly beyond help. And this last statement serves to illustrate our third reason, namely, that if it were not for tuberculin our treatment of these tuberculous conditions would be very unsatisfactory. Here were 30 patients who had had everything else done and were given up as beyond help, and they were improved with properly administered tuberculin. And one has only to think of one's own experience with cases of iritis and keratitis, where everything proper was done both locally and generally, which did not do well till tuberculin treatment was instituted. I have given at least 2,000 injections of tuberculin, and I have yet to hear of a case which I have harmed. Two of the opponents of tuberculin therapy, Derby and Carvill, say that the recovery is a result of psychotherapy and improved hygiene. I know that I myself have had cases (I am treating one now) whose hygiene is anything but good, but who have still done well on tuberculin. While I think we should try to improve their hygiene, I believe that these patients can get better without it when they are on tuberculin. And if not tuberculin — what? Will proper hygiene be sufficient? Will foreign proteins? I do not believe so. I must admit at this juncture that I have had no experience with any of the special rays or phototherapy.

TESTS USED IN THE DIAGNOSIS

I consider the Mantoux test as the best and most informative test. This consists of three intradermal injections of dilute old tuberculin and a control. The dilutions of the tuberculin are No. 5 solution, or 1:100,000, 0.1 c.c. of which contains 0.001 mg. tuberculin; No. 4 solution, or 1:10,000, 0.1 c.c. of which contains 0.01 mg. tuberculin; and No. 3 solution or 1:1,000, 0.1 c.c. of which contains 0.1 mg. tuberculin. These dilutions may be all given at once in a line up the arm, as we did at the Knapp Hospital, or they can be given separately as is done at the Wilmer Institute. Here they give the 1:100,000 dilution and wait 48 hours and then give the next strength if necessary, and then the next. While this is a very safe way it is time-consuming, and I have never seen any harm from giving the injections all at once. Of course if you get a response with the 1:100,000 dilution that is all you need. One-tenth of a c.c. is given

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intradermally, and this also applies to the control which is prepared with phenol the same way, but leaving out the tuberculin. There are occasional cases where you have the whole four injections showing a reaction. This we consider due to the phenol and that the test is of no value. Fortunately these are rare. The patients must report back in 24 and 48 hours, and careful measurements of the area of the reaction made. If the areas are over one cm. in diameter the test is considered positive. It is important not to miss the first day, because sometimes that may show more than the second, and the reverse may be the case. Some say that the Mantoux test should be done on a hospitalized patient but I see no objection to doing it on an ambulatory case. If this test does not give any information and you still feel the lesions are tuberculous the patient may be brought into the hospital and have a subcutaneous tuberculin test done. In this, careful observations of the temperature are taken every two hours for 24 hours, and then a subcutaneous injection of 1 mg. tuberculin (0.1 c.c. No. 2) is given and the same careful observation of the temperature is carried out for 48 hours. In considering the results the chart, local reaction, and focal reaction, if any, are taken into account. A focal reaction may be especially indicative, but this is undesirable, and efforts to produce this with larger doses of tuberculin are to be condemned. If this test shows nothing it may be repeated, using 2 mg., and while some authors advocate going higher I believe this is dangerous practice and that the results are not of as much significance.

In a recent series of experiments with rabbits, Woods, Burky and Friedenwald,[5] at the Wilmer Institute, were able to prove that the cutaneous sensitivity gives a fairly reliable index of the degree of ocular sensitivity in the systemically injected rabbit with undiseased eyes. Also that in rabbits which had had living tubercle bacilli injected into the anterior chamber, there was no relation between the cutaneous sensitivity and the sensitivity of the diseased eye. This would explain, I suppose, why we do not get the positive Mantoux tests that we expect sometimes.

CASES IN WHICH THE TESTS ARE MADE

Tuberculosis of the uveal tract is the commonest form of ocular tuberculosis. This may be a generalized uveitis, a choroiditis, an iritis, or an iridocyclitis. Every patient with uveitis should be studied with tuberculosis in mind when the investigation is being made. And when you consider it the proper time, *i.e.*, when other measures have been tried both locally and generally, and there is no contraindication, such as positive chest findings, a systematic course of dilute tuberculin injections should be instituted.

Sclerosing keratitis is usually due to tuberculosis. In my experience these cases have only done well when having tuberculin injections. Gifford[6] has watched cases treated with and without tuberculin, and he reports definitely in favour of tuberculin. Disciform keratitis is also often much benefited by tuberculin.

Scleritis and episcleritis often show the most dramatic improvement under tuberculin when everything else has been unsatisfactory. My feeling is that we should not long delay starting tuberculin in these cases as they are so frequently caused by tuberculosis. Oftentimes one small injection causes marked improvement.

Recurrent vitreous and retinal hæmorrhages—Eales' disease.—These cases usually occur in young males and most often in the left eye. This is due to a tuberculous involvement of the walls of certain of the retinal vessels. In Gay's[2] series of 30 severe cases 5 were in this group, and they were all benefited by tuberculin. Even cases where there was proliferating retinitis were improved. In using tuberculin in this condition a particular effort must be made to avoid a focal reaction, because a focal reaction in which the retina is concerned may do great damage to it. The treatment should be very cautious and prolonged, possibly for one to two years.

Phlyctenulosis is mentioned here, because, even though the tuberculous nature is recognized, tuberculin is to be avoided because of the danger of a focal reaction, and because it, unlike most of the other tuberculous eye conditions, responds much more readily to general hygienic measures.

ADMINISTRATION OF TUBERCULIN

In commenting on treatment with tuberculin I will confine my remarks to the only preparation I am familiar with, and that is old tuberculin. I will only mention the others. (1) Denys bouillon filtrate is preferred at the Wilmer Institute; (2) B.E. or Bacillen Emulsion; (3) Tuberculin A.O., the Japanese preparation; (4) Tuberculin M.A. 100; (5) Beraneck's tuberculin; (6) Tebeprotin.

I find the Connaught Laboratory Old Tuberculin very satisfactory both for diagnosis and treatment. At the Knapp Hospital we used the Old Tuberculin prepared by the City Health Department Laboratory. Once tuberculin is diluted it does not keep well. It should be kept in a cool place, and should be prepared at least once a month, although we used to prepare it once a week. It should be injected subcutaneously in the region of the deltoid muscle. The initial dose should be very small, because we do not know anything about the patient's sensitivity. We start with the 1:100,000 dilution, giving 0.2 c.c. While the patient is on this dilution and on 1:10,000 solution or bottles 4 and 5, he should have two injections a week. When he comes back, careful inquiry is made as to what the reaction was last time. If there has been a reaction at all, either local, general or focal, the next dose is not increased. In fact, if there has been a focal reaction the dose should be decreased. However, the possibility is that there has been no reaction, so the dose may be increased to 0.4 c.c. The dose is gradually raised each time until eventually 100 mg. is given, or 1 c.c. of bottle No. 1, or 1/10 dilution. When we reach bottle No. 3, or 1:1,000 dilution, we have them come once a week, and when we reach bottle No. 2 or 1:100 dilution, once in two weeks. When they are on bottle No. 1 we have them come once a month. It may have taken a long time, perhaps a year or more, to reach this strength, but this shows that we can gradually desensitize a person so that he can stand a dose which would ordinarily produce serious effects. Quite often the story is that the patient has cleared up long before this and does not see the necessity for continuing treatment. The patient should be under the observation of the ophthalmologist during his course of treatment. In fact, I believe that the treatment should be administered by the ophthalmologist because, ordinarily speaking, he knows most about it. Malignant exudative forms of tuberculosis should not be treated with tuberculin because of the danger of a focal reaction. One should use the form of tuberculin with which he is most familiar and not experiment with others.

CONCLUSION

In tuberculosis of the eye we are dealing with a special manifestation of the disease in which frank pulmonary tuberculosis is seldom present. I believe that in tuberculin we have a very valuable therapeutic aid provided that it is properly used in the right cases. I do not believe that there is anything to take its place in certain cases, and these should not be deprived of its benefits. The production of focal reactions is to be condemned, as a dose strong enough to cause this, apart from the harm it might do the eye, might light up a focus somewhere else. I do not believe that the ophthalmologist should "pass the buck" to someone else to carry out the treatment, but should do it himself and constantly have the eye under observation. Whereas, ordinarily speaking, it is advised to treat with other methods, such as removal of foci, etc., first, there are some cases, such as scleritis and typical nodular iritis with the slit-lamp, in which you are going to help your patient a lot more by not waiting too long to get started on tuberculin. If one constantly keeps in mind not to increase the dose if there is any kind of reaction, the possibility of producing harm is quite remote.

REFERENCES

1. WILMER, W. H.: Clinical aspects of ocular tuberculosis, *Arch. Ophth.*, 1928, 57: 1.
2. GAY, L. N.: Treatment of ocular tuberculosis with tuberculin, *Arch. Ophth.*, 1930, 3: 259.
3. ADLER, F. H. AND MEYER, G. P.: Tuberculous lesions of the uveal tract. A review of the literature, *Arch. Ophth.*, 1937, 18: 275.
4. PATON, R. T.: Recurrent retinal and vitreous hæmorrhage in the young, Eales' disease. Report of ten cases, *Arch. Ophth.*, 1938, 20: 276.
5. WOODS, A. C., BURKY, E. L. AND FRIEDENWALD, J. S.: (1) Relation of ocular sensitivity to cutaneous sensitivity in the systemically infected rabbit, *Arch. Ophth.*, 1938, 19: 229; (2) Relation of ocular activity to ocular sensitivity in the normal rabbit infected by injection of tubercle bacilli into the anterior chamber, *ibid.*, 1938, 19: 236; (3) Relation of cutaneous sensitivity to ocular sensitivity in the normal rabbit infected by injection of tubercle bacilli into the anterior chamber, *ibid.*, 1938, 19: 245.
6. GIFFORD, S.: A Hand-Book of Ocular Therapeutics, Lea & Febiger, Phila., 1932.
7. BERENS, C.: The Eye and its Diseases, Saunders, Phila., 1936, p. 832.

IRIDOCYCLITIS AND SECONDARY GLAUCOMA*

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THE co-existence of iridocyclitis and increase in ocular tension forms a very complex problem and one in which one must weigh the danger to the visual function from the two processes. In looking up some articles in the literature I found a good deal of discussion as to whether certain cases were primarily iridocyclitis with a secondary rise in tension, or primarily glaucoma with an iridocyclitis added. It would seem as if the same problem is involved, no matter which condition is primary, as each of the conditions is capable of producing serious damage to the vision.

A glaucoma is said to be secondary when there is some demonstrable condition present in the eye which is the cause of the rise in tension. Elliott, Duke Elder and others make the statement that the more glaucoma is investigated and the more it is understood, the more cases are found to be secondary and the fewer primary. It may even be that in some cases that are thought to be primary there is present a low grade iritis which may be a factor in the causation of the condition.

I would like to describe briefly three cases that I have had in the last year and a half, one of which came out badly, and the other two had a satisfactory result.

CASE 1

A patient, aged 69, had ordinary double senile cataract. The cataract in the right eye was removed with a good result, a perfectly normal course of healing, no complications, and a perfectly quiet eye. Three months later he reported with the left eye sore. The conjunctiva was inflamed and the cornea cloudy, with many spots on the posterior surface. The iris was muddy, thickened, and spongy in appearance, and had a good deal of exudate on the surface and in the pupillary area. There was, of course, a mature cataract. The tension was increased and with Schiotz tonometer measured 45 mm.

This was quite evidently a case of iridocyclitis with a secondary rise in tension. I first used eserine with no appreciable diminution in the tension and no decrease in the pain. I then used atropine; the pupil dilated only partially, and still the tension was very high and the pain not relieved. During this period he was given soda salicylate and codeine. The only focus of infection we could find was two teeth which were suspicious and were removed as a possible cause, but with no improvement in the eye. Then a paracentesis of the anterior chamber was done and atropine used. Of course the tension was relieved, but only for one day. The tension became high again and an iridectomy was done and atropine continued. The tension remained low after the iridectomy, but the eyeball became more painful and tender, and was eventually removed because of the pain and the fear of a possible sympathetic ophthalmia.

CASE 2

This patient, aged 60, was seen five years ago with an attack of iritis for which no cause could be found, but which cleared up rapidly with atropine and soda salicylate, and there was no rise in tension. In February of this year she reported with the eye sore again. On examination the conjunctiva was inflamed, the cornea showed numerous spots on the posterior surface in the typical triangular form, the iris was muddy showing some exudate in the pupillary margin, but the tension was high. The anterior chamber was not shallow.

This patient I immediately sent to hospital and did a paracentesis of the anterior chamber and started atropine. The pupil dilated with difficulty showing some adhesions to the capsule which gradually separated however. In twenty-four hours the tension was up again, the paracentesis wound was opened with a spatula, and the anterior chamber emptied again. In twenty-four hours the tension was up again and the anterior chamber fairly deep; the wound was opened again. The tension remained high, and I repeated this procedure for five days in succession. On the sixth day the tension was normal and has remained so. The K.P. gradually disappeared, the pupil was well dilated, and the eye continued to improve, became white and quiet, with no impairment of vision.

CASE 3

This was a young man who complained of pain in the eye. The conjunctiva was inflamed, the cornea showed a very few K.P., the anterior chamber was fairly deep, and the iris cloudy, with considerable exudate in the pupillary area which did not appear to be of recent origin. He gave a history of a previous attack of inflammation, which was evidently an iritis as the iris was adherent to the capsule of the lens and never did dilate. The tension was very high. I followed the same line of treatment, did a paracentesis, used atropine and soda salicylate and re-opened the wound every day for five days; on the sixth day the tension was normal. As I said before, the adhesion of the iris never did let go, as the pupil did not dilate, but the adhesion was evidently not complete as there was no iris bombe, and there must have been some circulation of the aqueous. In neither of these latter cases were we able to find a focus of infection as a cause.

These three cases, coming as they did close together, impressed me with the importance of adopting some very definite line of treatment and carrying it out boldly. Elliott says the decision whether to use myotics or mydriatics is so perplexing that some surgeons prefer to put their confidence in the general treatment, rest, purgation, etc., and to use no drops at all, or, as he suggests, try dionine. He recommends, however, that if there are definite signs

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of iritis atropine should be used freely, but the surgeon must be prepared to interfere surgically if the symptoms are not relieved soon, or if there is a considerable rise in the tension. If this occurs he suggests a sclero-corneal trephining, but says that with the iris in its inflamed condition the opening is very likely to become occluded at an early date. Tooke reports some cases in which he persisted in the use of atropine in spite of further rise in tension for ten days or more, and the iritis eventually cleared up and the tension then came back to normal with no damage to the vision. Elliott says "Iridocyclitis accounts for rise in tension by altering the character of the aqueous fluid and thus making it less fit for escape through the meshes of the pectinate ligament, and by furnishing the fluid with cells of inflammatory origin, which tend mechanically to block the open spaces of the filtration area. The angle of the anterior chamber may be completely closed by the contact of the root of the iris with the periphery of the cornea by inflammatory exudate."

In these cases, as in every inflammatory condition, exudation takes place, the production of the aqueous is increased, and it contains a large number of cells, chiefly lymphocytes. Their tendency to conglomeration was additional reason for interference with drainage.

It appears that the increase in tension is definitely associated with the iridocyclitis, the iridocyclitis being the primary factor and the increase in tension secondary. In treating such a hypertension it is necessary to treat the iridocyclitis which is the cause, and for this reason mydriatics appear to be definitely indicated. The first object is to dilate the pupil as much as possible, to remove the congestion from the iris and to rupture the synechiæ. On the contrary myotics may have an unfavourable effect on the inflammatory manifestation of the iridocyclitis. They aggravate the congestion of the ciliary body and favour the production of posterior synechiæ. By rupturing the posterior synechiæ mydriatics permit the free passage of the aqueous, and this largely explains the favourable effect of atropine on the ocular hypertension. Weekers has never observed an exacerbation of the hypertension in these cases after the use of atropine. He says "The use of atropine in this way causes the pressure to become normal in about half of the cases. When medical treatment is not successful in reducing the tension the visual function will be lost unless the tension is relieved promptly. This can easily be done by simple puncture of the anterior chamber, but its effect is transitory and the puncture must be repeated. Repetition of the puncture has a bad effect on the iritis."

I do not believe that re-opening of the paracentesis wound has any bad effect on the iritis. On the other hand, I believe emptying the anterior chamber and having it fill up with fresh aqueous humour has a beneficial effect, in the same way that in meningitis the removal of the cerebro-spinal fluid with formation of new fluid is beneficial.

Of course, in iridocyclitis one must always endeavour to find the cause, whether it is associated with an increased tension or not. We all know the different causes such as focal infections, syphilis, gonorrhœa, diabetes, tuberculosis, etc. The cause should be searched for and treated, quite apart from the local measures that are undertaken.

How often can a paracentesis be repeated? In one case recently I reopened the wound eighteen times over a period of three weeks. At the end of that time the edges of the corneal wound showed some exudate. Twenty-four hours after each reopening the edges of the wound were united, and on discontinuing this re-opening for a few days the corneal wound closed with no permanent change other than the small scar resulting from the incision.

My conclusion is that in these cases of glaucoma where an iritis is present, one should use atropine, and if on dilatation of the pupil the tension is not lowered promptly, a paracentesis of the anterior chamber should be done. This wound should be reopened repeatedly until by medical treatment and the treatment of any causative condition the iritis has subsided.

A SURVEY OF THE OPHTHALMIC CONDITIONS AMONG RURAL SCHOOL CHILDREN*

II.

BY JOHN V. V. NICHOLLS

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IN October, 1939, a survey was carried out to investigate the incidence of abnormal ophthalmic conditions among rural school children in Pontiac County, P.Q.[1] In May, 1940, another similar survey was carried out in this county and in Wakefield county. Again the pupils were examined without selection. In all some 512 children, 255 male and 257 female, between the ages of 5 and 18 years inclusive, were examined. As in the previous survey the eyes of each child were examined for any abnormalities in the anterior segment, adnexa, and extraocular movements. The visual acuity was recorded for each eye, using Snellen's test types at 20 feet, under proper illumination. Every child showing subnormal visual acuity, abnormalities of the anterior segment, or anomalies of the extraocular movements was examined further under the action of a cycloplegic. Refractive corrections, when given, were based upon retinoscopy carried out under the action of the cycloplegic.

The results of the present survey, when examined statistically, give some interesting comparisons with those of the previous one. In the table presented are recorded all the ophthalmological disturbances found. The sex and total incidence of each is listed.

Of the ophthalmic conditions found the most important and interesting comparisons are seen with regard to defects of vision. In the present survey 14.6 per cent of the children had subnormal visual acuity as compared with 29.7 per cent in the previous survey. A search for the reasons of this reduction discloses some interesting facts. It is found that the incidence of hypermetropia and hypermetropic astigmatism in the two surveys is almost identical. The same is true of anisometropia, which is another frequent cause of subnormal visual acuity. It is found that the lower incidence of subnormal

* Conducted under the ægis of the Quebec Division of the Junior Red Cross Society, and with the kind co-operation of the local school boards and medical practitioners.

TABLE I.

PATIENTS EXAMINED: TOTAL, 512; MALE, 255; FEMALE, 257

Number	Diagnosis	Male		Female		Total	
		Number	Percentage	Number	Percentage	Number	Percentage
1.	Blepharitis sicca	3	1.2	4	1.5	7	1.4
2.	Hordeolum	1	0.39	0	0	1	0.19
3.	Spastic entropion	0	0	1	0.39	1	0.19
4.	Phlyctenular conjunctivitis	1	0.39	0	0	1	0.19
5.	Corneal nebula	1	0.39	0	0	1	0.19
6.	Dermoid (corneo-scleral)	1	0.39	0	0	1	0.19
7.	Congenital cataract (stellate)	2	0.78	0	0	2	0.39
8.	Optic atrophy (primary)	0	0	1	0.39	1	0.19
9.	Enophthalmos (post-traumatic)	1	0.39	0	0	1	0.19
10.	Atrophia bulbi (post-inflammatory)	1	0.39	0	0	1	0.19
11.	Hypermetropia requiring correction	4	1.6	1	0.39	5	0.98
12.	Hypermetropic astigmatism	11	4.2	11	4.2	22	4.2
13.	Myopia	6	2.4	17	6.6	23	4.5
14.	Myopic astigmatism	3	1.2	7	2.7	10	1.9
15.	Mixed astigmatism	0	0	5	1.9	5	0.98
16.	Anisometropia of marked degree	6	2.4	5	1.9	11	2.1
17.	Strabismus, convergent monocular	1	0.39	2	0.77	3	0.51
18.	Strabismus, convergent alternating	2	0.78	0	0	2	0.39
19.	Strabismus, divergent monocular	0	0	1	0.39	1	0.19
20.	Strabismus, divergent alternating	0	0	2	0.77	2	0.39
21.	Convergence deficiency	0	0	4	1.5	4	0.78
22.	Subnormal visual acuity	33	12.5	42	16.3	75	14.6
23.	Subnormal visual acuity, non-correctable	16	6.3	15	5.9	31	6.1
24.	Patients wearing glasses	6	2.4	12	4.7	18	3.5
25.	Glasses worn but unnecessary	0	0	4	1.5	4	0.78
26.	Glasses ordered	11	4.0	23	8.9	34	6.6

visual acuity in the present survey is due entirely to the smaller number of cases of strabismus and myopia. There is a definite hereditary factor in both these ailments. A larger proportion of the children of the previous survey were related in some degree than in the present series. In the more detailed analysis carried out in the first survey it was found that myopia became less common, the younger the age-group. In the present series a greater proportion of the children belong to the lower age-groups. Apparently something else, statistically less definable, is operating. In the first survey fully one-half of the children examined attended Shawville High School, practically under urban conditions. Whereas, in the present series, much the larger proportion of children attended school under rural conditions. In some places it was found that school closed down during the severe winter months. In other words, the children in the previous survey were under a more continuous and determined educational drive than the children in the present survey. This has taken its toll in myopia.

In the two surveys glasses were prescribed in almost the same percentage of cases. However, fewer children were found already wearing glasses in the present series. In four such cases it was found that the glasses worn were not necessary. As in the last survey, a medical practitioner was not responsible for the mistake in diagnosis in any of these cases.

REFERENCE

1. NICHOLLS, J. V. V.: A survey of the ophthalmic conditions among rural school children, *Canad. M. Ass. J.*, 1940, **42**: 553.

RÉSUMÉ

En 1939 et 1940, 512 enfants des comtés de Pontiac et Wakefield ont subi des examens complets de la fonction visuelle. Ceux du comté de Pontiac ont été revus une seconde fois. Lors du deuxième examen, 14.6 pour cent avaient une acuité visuelle inférieure à la normale alors que les chiffres étaient de 29.7 pour cent au premier examen. Cette différence s'explique par la diminution du strabisme et de la myopie, les autres états étant à peu près les mêmes. Dans la première série, plus d'enfants étaient unis par des liens de parenté que dans la deuxième série. Les enfants examinés en 1940 étaient proportionnellement plus jeunes. En 1939 on retrouvait plutôt des conditions de vie urbaine tandis que celles de 1940 se rapprochaient davantage des conditions rurales. L'étude prolongée paraît augmenter la proportion des myopes. Les verres ont été prescrits également en 1939 et 1940. Quatre enfants les portaient inutilement.

JEAN SAUCIER

ANÆSTHESIA IN THE PATIENT WITH PULMONARY TUBERCULOSIS*

BY H. E. PUGSLEY AND G. D. RICHARDSON

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PATIENTS with active pulmonary tuberculosis usually tolerate anæsthesia and operation very well. However, a small percentage develop a post-operative spread of the tuberculous disease in their lungs. This extension of the pulmonary lesion is the principal cause of post-operative deaths and it is the purpose of the present paper to indicate the causes of and measures which will aid in the prevention of this serious complication. Overholt[1] reported a mortality within three months of thoracoplasty of 2.2 per cent in a large group of patients under forty years of age, and a mortality of 6 per cent in a group over forty years of age. In both groups, the principal cause of death was an extension of the tuberculous process within the lung.

We believe that surgical shock results in a lowered resistance to the tuberculous infection and is one of the primary causes of a spread in the lung. Therefore, every effort should be made to avoid the development of shock by careful pre-operative preparation, multiple stage operations where feasible, routine intravenous saline during major surgery, and blood transfusion if signs of shock appear.

THE SELECTION OF THE ANÆSTHETIC

Local anæsthesia is selected for most minor operations, such as the insertion of an intercostal catheter or intrapleural pneumolysis. For such minor procedures as the opening of an ischio-rectal abscess we have found pentothal sodium given intravenously very satisfactory. This agent causes no pulmonary irritation or stress, the patient emerges from the anæsthetic quickly, and is rarely nauseated afterwards.

For major operations below the level of the diaphragm spinal anæsthesia is usually selected. For short operations we use procain and for

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those of longer duration, nupercain. These agents provide satisfactory analgesia, respirations are quiet, and the cough reflex is not abolished.

For major thoracic operations, such as thoracoplasty and extrapleural pneumolysis, we prefer cyclopropane anæsthesia. Alexander,[2] in discussing the selection of the anæsthetic agent for thoracoplasties, states, "There is no available evidence to show that a properly administered gas anæsthetic is responsible for a higher percentage of post-operative complications than is local anæsthesia and, in fact, it is probably responsible for a lower percentage, whether the patient's sputum be little or great in amount." Dunlop[3] states that inhalation agents "remain the most generally useful in major thoracic surgery" and that "by all odds, the most popular inhalation agent now in use is cyclopropane". Shields[4] also selects this gas for thoracoplasties. The many advantages of cyclopropane with its high oxygen content, quiet respiration, quick action, and only slight irritation of the respiratory membrane, are well known.

THE PRE-OPERATIVE PREPARATION OF THE PATIENT

Patients with pulmonary tuberculosis in the acute exudative phase should, if possible, have a long period of bed rest until the lesion is in a more chronic fibrotic phase before being subjected to a major operation. It is known that a post-operative spread of the tuberculous process in the lung occurs much more frequently in the former than in the latter stage. Patients should be encouraged to "empty the lungs" of all available secretions by coughing and postural drainage during the few hours preceding operation. Those with profuse expectoration should not be operated on early in the morning before they have had ample time to clear their lungs of secretions.

Liberal quantities of fluids and glucose should be given during the twenty-four hours preceding operation. An intravenous infusion of normal saline is a routine measure before all major

TABLE I.
MUSKOKA HOSPITAL
ANALYSIS OF ANÆSTHETICS FOR 147 MAJOR OPERATIONS ON 82 PATIENTS WITH PULMONARY TUBERCULOSIS

Anæsthetic	*Number of operations*	*Surgical shock*	*Post-operative spread in the lung within 3 months*	*Post-operative deaths within 3 months*
Cyclopropane	127 (118 major chest operations.)	13	5 (All followed major chest operations and 3 of the 5 had surgical shock.)	3 Tuberculous pneumonia... 1 Influenza pneumonia..... 1 Tuberculous cellulitis..... 1
Spinal	20	0	2 (One was a terminal case.)	2 Terminal tuberculosis..... 1 Streptococcal peritonitis... 1
Totals.....	147	13	7 Excluding the terminal case; Operation incidence 4.1% Case incidence..... 7.3%	5 Excluding the terminal case; Operation mortality... 2.7% Patient mortality..... 4.9%

NOTE.—71 per cent of the above patients had sputum positive for tubercle bacilli at the time of operation.

TABLE II.
MUSKOKA HOSPITAL
ANALYSIS OF ANÆSTHETICS FOR 75 MINOR OPERATIONS ON 35 PATIENTS WITH PULMONARY TUBERCULOSIS

Anæsthetic	*Number of operations*	*Surgical shock*	*Post-operative spread in the lung within 3 months*	*Post-operative deaths within 3 months*
Cyclopropane	18	0	0	0
Spinal	12	0	0	0
Nitrous oxide	6	0	0	0
Intravenous pentothal or evipal	39	0	1 Terminal tuberculosis	1 Terminal tuberculosis
Totals.....	75	0	1	1

NOTE.—33 per cent of the above patients had sputum positive for tubercle bacilli at the time of operation.

surgery, and is continued during and after the operation until the patient has received about three litres of fluid. This measure tends to eliminate shock and may be a factor in the reduction in the incidence of atelectasis by preventing the pulmonary secretions from becoming too viscid.

A sedative such as pentobarbital sodium is prescribed on the night preceding operation. One hour before operation, pantopon, gr. 1/3 with hyoscine gr. 1/150 is given by hypodermic, followed in fifteen minutes by pentobarbital sodium, gr. 1½ to a man of average size; women receive slightly smaller doses. The patient usually arrives in the operating theatre either asleep or free from apprehension.

Before major surgery the patient's blood should be typed with that of a prospective donor in order that a blood transfusion may be given immediately following operation should signs of shock appear. In addition, a blood transfusion is indicated for patients with a hæmoglobin of less than 70 per cent.

Operative Complications During Major Chest Surgery

During major chest surgery there are certain operative complications worthy of note, and measures which will aid in their prevention or control are indicated below.

Troublesome reflexes such as breath-holding or laryngospasm are prone to develop when the periosteum is being stripped off the rib or the parietal pleura from the chest wall in a patient too lightly anæsthetized. This breath-holding or stridor causes anoxæmia, rapid pulse rate, increased venous pressure, and may contribute to the development of shock. To avoid these reflexes cyclopropane anæsthesia is induced at least ten minutes before the surgeon begins to operate and is deepened to about the second plane of the third stage. When the surgeon commences to close the muscle layer the anæsthetic is lightened by the addition of air or a helium-oxygen mixture. If the above technique is followed intubation for thoracoplasty becomes necessary in only a small percentage of cases, chiefly those requiring tracheal aspiration because of profuse pulmonary secretions.

Paradoxical respiration commonly occurs and may become quite marked during the operation of extrapleural pneumolysis and less so during a thoracoplasty. Occasionally an accidental pneumothorax will develop during the former operation; rarely, during the latter. Both complications are aggravated by a partial obstruction of the airway and, therefore, the endotracheal catheter technique is recommended as a routine for extrapleural pneumolysis; this technique also ensures that the patient will not have expiratory stridor, which causes the lung to balloon out into the surgeon's field of operation during the stripping of the parietal pleura off the chest wall. Rhythmic pressure on the breathing bag may be necessary to relieve anoxæmia as a result of paradoxical respiration in a patient with limited respiratory reserve.

Obstruction of the airway by pulmonary hæmorrhage or excessive secretions is a rare complication. Nevertheless, facilities for tracheal aspiration through a catheter or bronchoscopic aspiration should be immediately available.

The importance of avoiding surgical shock as well as measures of prevention and treatment have been stated. The anæthetist should be alert for early signs of shock such as falling blood pressure and increasing pulse rate. When these appear the surgeon is at once notified so that he may consider immediate closure and completion of the operation at a later stage.

Post-operative Complications

The complication responsible for most post-operative deaths in this group of patients is an extension of the tuberculous process in the lung, either as a bronchogenic spread due to aspiration of infected secretions or as an acute exacerbation of a pre-existing focus in the lung. To reduce the incidence of this serious complication to a minimum, patients whose pulmonary lesion is in an acute exudative phase should, if possible, have major surgery postponed until rest treatment has resulted in the body temperature returning to normal or nearly normal and the x-ray shows evidence of fibrosis or "hardening" of the lesion. Other factors in its prevention are a strict observance of the measures of pre-operative preparation and the avoidance of surgical shock.

During the few days immediately following a thoracoplasty in which too many rib segments have been removed paradoxical respiratory movements of the weakened chest wall may lead to increasing exhaustion and a terminal tuberculous pneumonia. By limiting each stage of the operation to the removal of about three ribs this complication is rarely seen.

Patients with tuberculous empyema and a broncho-pleural fistula form a very hazardous group because of the high incidence of a bronchogenic spread of the tuberculous process following operation. All patients with tuberculous empyema should have a thorough aspiration and washing out of the pleural cavity shortly before operation, because an intermittent bronchopleural communication may be present in the absence of any clear clinical indication of such. If a secondary infection is present in the empyema sac pre-operative intercostal drainage and irrigation is indicated.

Atelectasis of a lobe or whole lung may develop if a plug of mucus becomes lodged in a bronchus, although this is not a common complication. A liberal intake of fluids probably aids in its prevention by keeping pulmonary secretions from becoming too viscid. When atelectasis develops, however, bronchoscopic aspiration of a mucous plug should be attempted.

Table I and II are an analysis of anæsthetics for 147 major operations and 75 minor operations at the Muskoka Hospital. It is noteworthy that no complications followed the minor operations except in one case of terminal tuberculosis. This may be taken as evidence that surgical shock and trauma are important factors in the causation of post-operative spread of the pulmonary lesion.

Figs. 1 to 4 illustrate certain points mentioned in the text.

CONCLUSIONS

1. The most frequent serious post-operative complication in this group of cases is an extension of the tuberculous process in the lung.

2. The cause of and measures which tend to reduce the incidence of the above complication have been indicated.

3. Shocked patients run an increased risk of spread of the pulmonary lesion.

4. Patients whose pulmonary disease is in the chronic fibrotic phase usually tolerate anæsthesia and operation very well. Those with a lesion in the acute exudative phase are much more prone to develop a post-operative spread.

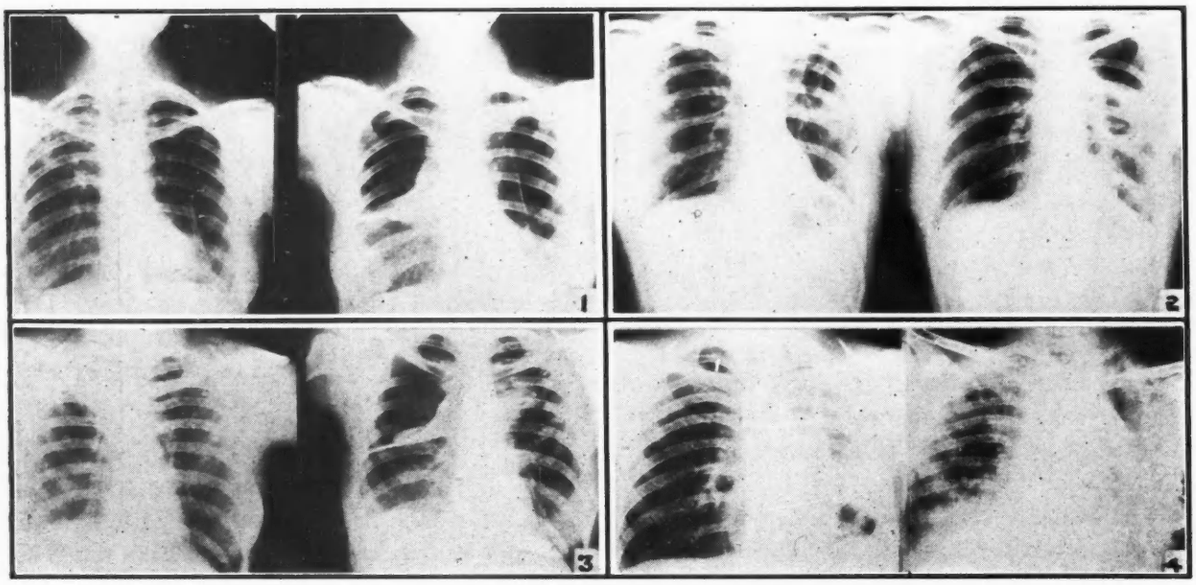

Fig. 1.—This illustrates the chest x-rays before and after extrapleural pneumonolysis on the right side done in the presence of artificial pneumothorax on the left. The endotracheal catheter technique is recommended as a routine for this operation. **Fig. 2.**—This is a case of a bronchogenic spread to the left lower lobe following an extrapleural pneumonolysis performed under local anæsthesia. We believe that the danger of a spread is just as great following major surgery done under local anæsthesia as it is under general anæsthesia with cyclopropane. **Fig. 3.**—An example of an acute flare-up of a focus in the left lung following an operation in which the patient developed surgical shock. **Fig. 4.**—This demonstrates a tuberculous bronchopneumonia in the right lung a few days after the first stage of a thoracoplasty on the left side in a patient with tuberculous empyema and a broncho-pleural fistula. The patient died on the seventh day and the above diagnosis was verified at autopsy.

The authors wish to express their indebtedness to Dr. H. J. Shields, Toronto, for his advice in the preparation of the above paper.

REFERENCES

1. OVERHOLT, R. H.: Thoracoplasty in older patients, *Am. Rev. Tuberc.*, 1940, **41**: 143.
2. ALEXANDER, J.: The Collapse Therapy of Pulmonary Tuberculosis, C. C. Thomas, Springfield, 1937, p. 443.
3. DUNLOP, J. G.: Anæsthetic practices in thoracic surgery, *Current Researches in Anæs. & Anal.*, 1939, **18**: 301.
4. SHIELDS, H. J.: Anæsthetic procedures as standardized for certain types of operation in a large general hospital, *Canad. M. Ass. J.*, 1938, **38**: 155.

A CLINICAL STUDY OF THE INFERIOR TURBINATE CAVERNOUS TISSUE; ITS DIVISIONS AND THEIR SIGNIFICANCE*

By Howard H. Burnham, M.B.(Tor.)

Toronto

THE cavernous tissue blood vessels of the lateral nasal wall have been regarded as a sheet of connecting vessels which may contract as a whole or in part in an unrelated and erratic manner. Anatomical investigation of the cavernous tissue of the lateral nasal wall has brought to light that the blood flows into a system of underlying vessels which in turn traverse bony canals in the turbinate. These vessels follow such definite courses as to suggest that certain blocks of cavernous tissue might react as units physiologically. The experiments which are described in this paper show that the cavernous-tissue vessels of the inferior turbinate act together in certain definite tracts or pathways which correspond with those noted in the anatomical work. Some clinical conclusions are drawn with regard to the part played by this mechanism in producing hypertrophy. The effect of cavernous-tissue reactions on the maxillary antrum circulation is indicated and the inadvisability of removing the anterior tip of the inferior turbinate. Reference is also made to the fallacy of certain commonly used physiological measurements of cavernous tissue reactions.

There is little to be found in the literature on this subject. So far as the writer is aware, no other anatomical work has brought out these interesting pathways and no physiological investigation has been undertaken regarding the vessels of the lateral nasal wall with this end in view.

Anatomy

The anatomy of the inferior turbinate venous channels has already been dealt with at considerable length in a previous communication. The accompanying diagrams indicate the different tracts or pathways dealt with in the following experiments.

We have found that the cavernous tissue of the inferior turbinate can be divided into three main areas or pathways which will be called A, B, and C. "A" is subdivided into four areas and "B" into two (Fig. 1).

Area "A" comprises the anterior 2/5ths of the inferior turbinate and the atrium area. The anterior 2/5ths of the inferior turbinate division measures about 2 cm. in length. Area "B" occupies the middle 1/5th of the inferior turbinate and Area "C", the posterior 2/5ths of the turbinate.

These three pathways correspond to certain vascular areas fairly well defined anatomically. In Area "A" the turbinate arteries have left their bony canals and the main branches lie in the periosteum only. The cavernous tissue is thick over this area.

Area "B" contains the anterior part of the bony canals of the inferior turbinate (Fig. 2B) and at the junction of areas "A" and "B" the arteries emerge from their bony canal orifices. The layer of cavernous tissue is thinner than in Area "A".

Lastly, Area "C" takes in the posterior 2/5ths of the inferior turbinate and includes the posterior tip. The cavernous tissue in this latter area is capable of marked dilatation and contraction (Figs. 2C and 2D).

Subdivisions of Areas "A", "B", and "C".

A1 is the name which we have given to a circular area of cavernous tissue at the extreme anterior tip of the inferior turbinate and close to the skin margin. It is about 1 cm. in diameter and lies anterior to the pyriform aperture. It is lying, therefore, on soft tissue and connects with the veins of both turbinate and face.

A2 is located between A1 and B1 and lies along the medial surface of the turbinate (Fig. 2A).

A3 comprises the atrium area.

A4 is the area of cavernous tissue along the inferior border of the turbinate between A1 and B2 areas, meeting the latter (B2) at a canal orifice through which passes the artery to the inferior border of the turbinate in its anterior 2/5ths.

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Area "B" is made up of two parts.

B1 is the area occupying the medial surface of the middle 1/5th of the turbinate (Fig. 2B).

B2 is located along the inferior border of the turbinate in this same area.

Area "C" is found posterior to Area "B", including the cavernous tissue of the posterior part of the turbinate which hangs down in a somewhat pendulous manner when fully dilated. It is this appearance which is used to illustrate the posterior tip of the inferior turbinate in most anatomical illustrations (Figs. 2C and 2D).

METHOD

The experiments have been of such a simple and non-injurious nature that human material has been used.

A small cotton applicator is dipped in a 3 per cent aqueous solution of ephedrine and lightly applied to the surface of the turbinate on a very small part of the pathway to be tested. It should not cover more than about 1 mm. This means that about 1 min. of the drug is actually acting on the area. The colour and size of the superficial vessels can then be observed through a 10 dioptre lens held close to the nasal speculum.

Of three factors which influence movement of blood in veins, namely, *vis a tergo*, gravity, and extrinsic muscle, two have been controlled by making them either a constant factor or by noting the change in capillary colour. Extrinsic muscle is, of course, not found in the mucous membrane of the nasal cavity or sinuses,

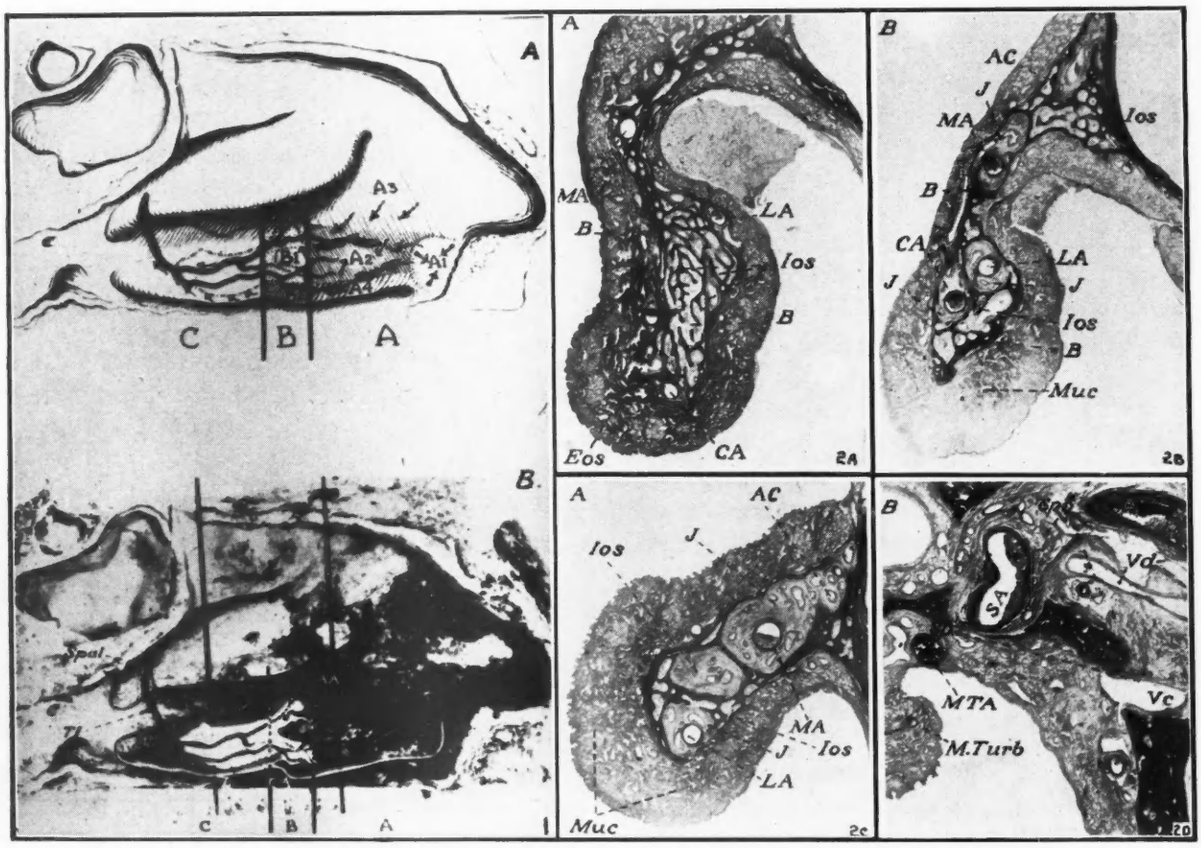

Fig. 1A.—This diagram, traced from the photog raph of the lateral nasal wall below, shows the cavernous tissue divisions A, B, C and the subdivisions. The arrows indicate the direction of venous blood flow. The point of some arrows is blunted, indicating that blood is also flowing into tiny bony canals in addition to the main flow. **Fig. 1B.**—The white patch over the inferior turbinate indicates the area of the large bony canals for transmission of the large turbinate vessels. The cross sections of the turbinates in Figs. 2A, 2B, 2C and 2D were taken from this specimen. **Fig. 2A.**—(Mag. 7X.) Cross section through division A, *i.e.*, anterior half of inferior turbinate, showing the "intraosseous" canals and veins within them. The medial and lateral branches of the inferior turbinate artery are lying on the surface of the bone. A plexus of periosteal veins is seen about them. Some connections of erectile tissue with "intraosseous" veins can also be seen. **Fig. 2B.**—(Mag. 7X.) Cross section through division B, *i.e.*, inferior turbinate in its central one-fifth. The arteries noted in Fig. 2A are now in canals. **Figs. 2C and 2D.**—(Mag. 7X.) Cross section through division C of the inferior turbinate. The "canal for the antrum vessels" communicates with the superior canal.

Lettering: A.C., canal for antral vessels; Muc., mucoperiosteum; Ma., medial branch; La., lateral branch; J., a periosteal "jacket plexus" within a canal; B., bone; Ios., "intraosseous" veins and canals; Ca., communicating branch joining medial and lateral arteries; Eos., a connection between erectile tissue and an "intraosseous" vein. (Republished with permission from the *J. of Laryngol. & Otol.*, 1935, **50:** 569.)

a fact which Zuckerkandl stated in his very valuable paper of fifty years ago.

The patient is seated in the chair as for an ordinary rhinological examination. The head is kept still, thus eliminating the gravity factor as a cause of variation of the blood flow in the vessel reactions. The reaction of the cavernous tissue has been judged by the thinning or swelling of the mucosa, and the colour and dilatation of the surface capillaries has indicated any increase in arterial blood flow.

Anterior rhinoscopy has been carried out, noting the thickness of the inferior turbinate mucosa and relating it to other parts of the nasal cavity, to prevent any misconception of reactions which might take place. In every case it was found necessary to note whether or not shrinking took place after introduction of the nasal speculum. Not infrequently, within a few seconds of the introduction of the speculum, an inferior turbinate would be seen to shrink appreciably. Presumably this was due to the stimulating effect of the inspiratory current of air striking the surface of the mucosa more directly than with undilated nasal vestibule.

If a cotton applicator was to be used in applying the drug to the mucosa, the "pressure stimulus" was noted. This test consisted in touching the mucosa with a pressure equal to that which would be used in applying the drug. The reaction of the mucosa as regards colour and shrinking was then noted. By this means a fairly accurate idea was gained of the action of the drug itself. The best drug for stimulating the pathways to activity was found to be a 3 per cent aqueous solution of ephedrine. It allowed the blood to flow through the capillaries with little or no interruption. It caused contraction of the cavernous tissue, and there was seldom evidence of arterial dilatation. This latter statement has already been discussed in a former paper[2] and further work is being undertaken along these lines as opportunity offers.

Considerable time was spent in observing the "pathway" reactions. For a satisfactory test the turbinate must be reasonably swollen, otherwise the shrinking could not be noted with certainty. In other cases the turbinate was so hidden in whole or in part that again the reaction could not be seen well enough to give conclusive evidence. The experiments described below presented te necessary reactions clearly enough to be used as proof of the venous pathway reactions.

Posterior rhinoscopy was employed when necessary to observe the posterior tip of the inferior turbinate and to note any shrinking reaction.

EXPERIMENTS

A number of experiments have been carried out with the object of stimulating the various pathways of the inferior turbinate alternately and systematically in order to estimate by this means the effect of one upon the other. Owing to the difficulties of stimulating the posterior half of the inferior turbinate with ephedrine without also depositing the drug on the other pathways in the process it has taken time and patience to finally procure the ideal cases in which all these sources of error could positively be eliminated. A few typical cases have been chosen to illustrate the reactions.

Experiment 1.—Miss Q. On nasopharyngeal examination the posterior tips of both inferior turbinates were clearly seen. They were pale and presented the slightly mulberry appearance usually associated with hypertrophy. After shrinking down in the course of the experiment the right posterior tip showed no hypertrophy and the left shrank sufficiently to indicate a definite posterior tip reaction.

On dilating the vestibule with the nasal speculum, the anterior half of both right and left inferior turbinates in turn shrank slightly. After withdrawing the speculum and then re-introducing it the turbinate was found to have assumed its original thickness in the interval, but almost immediately shrank as before. This "speculum reaction", as I have called it, was therefore taken into consideration when drug reactions were noted.

3.12 p.m.—Ephedrine (3 per cent aqueous solution) applied to A1 area of right inferior turbinate.

3.13.—Shrinking has occurred over A1 area of turbinate.

3.15.—Shrinking has spread posteriorly along A2, and the anterior edge of division "B" is defined as a definite ridge.

3.19.—The inferior border of the turbinate, A4, has shrunken slightly, but to a much less degree than A2. This shrinking has now apparently ceased.

3.21.—Ephedrine is now applied to the inferior border of the turbinate, *i.e.*, A4.

3.22.—A4 is now markedly shrunken, *i.e.*, as far as the B2 area.

3.25.—Ephedrine applied to B2 area.

3.26.—B2 area is markedly shrunken.

Summary.—(1) Areas A1 and A2 have reacted together, shrinking in an antero-posterior direction and including area A4, *i.e.*, the anterior half of the inferior border, to a very minor degree. (2) The A4 area required a separate application of the drug to bring about a similar degree of reaction. (3) Area B2 required a separate application of ephedrine to bring about shrinking.

Conclusions.—(1) Areas A1 and A2 have responded together. (2) A4, *i.e.*, the anterior half of the inferior border, has reacted as a unit or separate pathway. (3) B2, *i.e.*, the inferior border of the "B" area has reacted as a unit or tract.

Remarks.—The combined reaction of A1 and A2 is not uncommon, although A1 area has frequently been observed to shrink without any effect on A2 (see Experiment 2).

Experiment 2.—Miss Q. (same case, next day). Posterior tips of inferior turbinate examined as in Experiment 1, and a similar condition found today. Similar preliminary tests were also carried out.

3.17.—Ephedrine is applied to A1 area of left inferior turbinate.

3.20.—A1 area of turbinate is shrunken. A2 is unaffected. On nasopharyngeal examination, no difference noted in posterior tip of turbinate.

3.23.—Ephedrine applied to A2 area of left inferior turbinate.

3.24.—A2 is shrinking slowly.

3.25.—Ephedrine applied again to A2.

3.28.—A2 is now markedly shrunken. Posterior tip of inferior turbinate is unaffected.

3.30.—The anterior border of the B1 area now stands out distinctly and A1 and A2 areas are flat. There is no change in posterior tip of left inferior turbinate.

3.35.—B1 area is slightly thinner. A4 area, *i.e.*, the anterior half of the inferior turbinate border is slightly thinner. B2 is unaffected. Posterior tip of turbinate is unaffected.

3.42.—Ephedrine applied to B1 area.

3.44.—Ephedrine again applied to B1 area.

3.45.—B1, *i.e.*, medial surface of "B" area, is shrinking.

3.49.—The posterior tip of the inferior turbinate is now appreciably shrunken for the first time.

Summary.—(1) A1 area reacted by itself and had no appreciable influence on A2. (2) A2 reacted by itself and had no appreciable influence on either "B" area or the posterior tip. (3) B1 area reaction included the posterior tip of the inferior turbinate.

Conclusion.—(1) The tracts of the inferior turbinate require separate stimulation to produce the full effect of the drug. (2) The tracts may react separately. (3) The shrinking of area "A" did not induce shrinking of the posterior tip of the turbinate.

Remarks.—The inferior border of the turbinate in this case may have been directly affected by excess of the drug. The inferior border is, as a rule, but little affected by the reaction of A2 and A1 tracts.

Experiment 3A.—M.S. This case was a particularly suitable one for these pathway tests owing to a very large septal perforation which made it possible to obtain a lateral view of the medial surface of the inferior turbinate in the "B" area on looking through the septal perforation. The posterior tip could also be partly made out. The usual preliminary tests were carried out.

2.35.—Ephedrine is dropped on the right inferior turbinate posterior to the "B" area. This is easily accomplished by passing the dropper through the septal perforation, thus avoiding any disturbance of the turbinate anterior to this.

2.36.—A2 is definitely shrinking.

2.39.—Ephedrine dropped over "B" area and posterior to it.

2.40.—The mucosa of the "B" area is slightly thinner.

Note.—The speculum stimulus is present, although lost for a few minutes after the posterior tip was shrunken. However, following the application of the drug to the "B" area, A2 has become markedly shrunken and the speculum stimulus is lost.

2.44.—The "B" area is now much thinner.

2.49.—The A2 is still markedly shrunken.

Summary.—(1) Application of ephedrine to the posterior tip caused marked shrinking of A2 area. (2) The posterior tip had practically no effect on the "B" area, although A2 was definitely affected. (3) Shrinking of "B" area with direct application of ephedrine caused a much more marked thinning of A2 than when the posterior tip alone was stimulated.

Conclusions.—Application of ephedrine to the posterior tip of the inferior turbinate affects A2 area of the inferior turbinate cavernous tissue pathways to a very definite degree. "B" area was but little affected in this experiment. Stimulation of the "B" area with ephedrine causes marked constriction of A2 area although the reverse does not apply.

Experiment 3B.—M.S. (the same patient). The left inferior turbinate was tested as described in experiments 1 and 2, with similar results.

Experiment 4.—Mrs. T. The posterior tips of the inferior turbinates could not be as clearly seen in this case, but during the experiment the effect of a postnasal application of ephedrine, *i.e.*, to posterior turbinate tips on the areas A2 and A1, was definitely noted.

2.38.—A postnasal application of ephedrine is made by the nasopharynx.

2.40.—Areas A2 and A1 of the right inferior turbinate are definitely shrunken more than was the case from the speculum stimulus alone and the shrinking is quicker. After removal of the speculum the turbinate again swells but again responds as before on the introduction of the speculum.

The patient's nose and front part of her head feel "clearer" since the nasopharyngeal application.

Experiment 5.—Mrs. T. The usual tests of pressure and speculum reflex were carried out.

2.10.—Ephedrine applied to A4, *i.e.*, the inferior border of the left inferior turbinate close to its anterior extremity.

2.15.—A4 area, *i.e.*, the inferior border, is shrunken back as far as the B2 area. The A1 tract is unaffected. The A2 tract is shrunken in this case.

2.18.—Ephedrine applied to the anterior part of B2, *i.e.*, inferior border of "B" area.

2.19.—This part of the inferior border of the "B" area is shrunken. The inferior border of the turbinate posterior to B2 is still unaffected.

2.32.—Ephedrine is applied to A1 area, which shrinks.

2.35.—Ephedrine applied to A3, *i.e.*, the atrium area, which has been unaffected so far. It shrinks.

Summary.—(1) A4, *i.e.*, the anterior half of the inferior border of the turbinate, shrinks, affecting A2 area. (2) B2 area, *i.e.*, inferior border of turbinate, shrinks alone. (3) A3, *i.e.*, atrium area, in this case shrinks only after a direct application to it.

Conclusions.—(1) A4, *i.e.*, anterior part of inferior border of turbinate, shrinks as a tract but in this case the reaction also includes the A2 area. (2) The A1 area reacts as a separate tract. (3) A3, *i.e.*, the atrium area, reacts as a separate tract in this case.

SUMMARY

1. The cavernous tissue of the inferior turbinate is composed of definite pathways or tracts which may react separately or synchronously. They correspond to the anatomical distribution of the cavernous tissue pathways. The periosteal veins are concentrated about the larger arterial branches to a great extent. The large arterial branches therefore indicate in a general way the location of those veins into which passes the blood from the cavernous tissue pathways A, B, and C.

2. The cavernous tissue tracts do not contract systematically in an antero-posterior direction, but the C pathway after ephedrine stimulation causes a shrinking of area A. As a rule, the block of cavernous tissue forming B area is little affected by ephedrine applied anterior to it, and, conversely, ephedrine applied to the posterior tip may affect A2 and A1 areas with no apparent effect on the cavernous tissue of B area. These reactions suggest that the stimulus is in the

nature of a vasomotor one, acting through the vessels in the bony canals.

CLINICAL CONSIDERATIONS

The clinical application of the foregoing physiological reactions is of interest.

A posterior turbinate tip application will have a marked effect on the cavernous tissue in area A, but area B may be little or not at all affected. The reverse, however, is not true, *i.e.*, under normal conditions of strain on area A, according to the foregoing experiment. External stimuli such as the inspiratory air current, etc., do not necessarily affect all the pathways of the inferior turbinate system equally or synchronously. For example, A1 area may be affected alone or A1 and A2 together. A3 may or may not be included in the reaction. Area B often gives no evidence whatever of a reaction when A1 and A2 tracts shrink.

It will be understood from this illustration how inaccurate may be the results of physiological experiments if the contraction or swelling of the nasal cavernous tissue is estimated by a measurement of the variation in the total air volume in a nasal cavity and no careful inspection of the nasal turbinates is carried out.

Hypertrophies of the mucous membrane commonly occur at areas of greatest strain on these cavernous tissue tracts. (*a*) A1 is the most exposed of all the tracts. (*b*) A4 is often involved, being at the most dependent part of the turbinate and with the added factor of suddenly restricted blood flow into the bony canals of area B2. (*c*) A localized hypertrophy is often found at the junction of A4 and B2, where a large bony canal orifice is found. (*d*) The posterior tip hypertrophy requires a little more detailed explanation.

We have shown the marked shrinking effect produced on area A by contraction of area C. This suggests that a very powerful shrinking effect is exerted on the cavernous tissue of area A by that of C. It may be considered in the nature of a reserve power which can be exerted on area A. It is a force to be called into action when area A is hard pressed or fatigued. Hypertrophies of the posterior tip therefore may indicate overstrain of cavernous tissue in area A and probably a more direct and potent cause of this hypertrophy than the irritation resulting from nasal discharge over the surface of the posterior tip.

Some of us have observed on numerous occasions that cavernous tissue of the posterior tip may be so contracted that the mucosa is almost as thin and pale in appearance as that of a normal sinus. At the same time areas A and B will present the normal thickness and pinkish-red appearance of a normal turbinate. It is evident that the normal circulation and reactions of Areas A and B can be carried on without any appreciable influence on the posterior tip. It is concluded, therefore, that the posterior tip influence on areas A and B is not called into action under average conditions but only when the latter are under extra strain.

The foregoing has brought out the influence of area C on area A through the bony canal route. A similar canal for transmission of veins from the *maxillary antrum* is found in the posterior 2/5ths of the turbinate in close communication with those from area A of the turbinate (Figs. 2C and 2D). We therefore conclude that the cavernous tissue of area C can exert a powerful constriction on the plexus of veins on the medial wall of the antrum.

Removal of the anterior tip of the inferior turbinate surgically has not infrequently been observed to produce much discomfort to the patient subsequently. A watering of the nose is one of the most annoying symptoms. We can now understand how such a careless removal of the cavernous tissue in this area interrupts the smooth co-ordination of one pathway with the other, and how a shutting-off of the outflow of blood through turbinate channels has left sensitive cavernous tissue exposed to external atmosphere without sufficient reserve to withstand these demands.

My thanks are due to Dr. Duncan Graham, Professor of Medicine, for the co-operation of his Department in this work.

REFERENCES

1. BURNHAM, H. H.: An anatomical investigation of blood vessels of the lateral nasal wall, etc., *J. Laryngol. & Otol.*, 1935, **50**: 569.
2. *Idem*: Some difference in the action of ephedrin and epinephrin on the nasal turbinate mucosa, *Canad. M. Ass. J.*, 1932, **27**: 168.
3. *Idem*: Headache from the nasal wall, *Ann. Otol., Rhinol. & Laryngol.*, 1937, **46**: 69.

OSTEITIS DEFORMANS (PAGET'S DISEASE)

BY M. SIEGEL

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OSTEITIS deformans was first described by Sir James Paget in 1876 as a "rare and strange malady of bones". Since that time many cases of osteitis deformans have been recorded in the literature, yet the condition still belongs to the rare diseases.

Carman and Carrick have found 15 cases in 237,000 admissions to the Mayo Clinic in six years. F. C. Newton[6] has found 17 cases of osteitis deformans in 40,000 admissions to Peter Bent Brigham hospital in ten years. Sugarbaker[7] has found 51 cases of Paget's disease in a total of 222,676 admissions to the Henry Ford Hospital from 1922 to 1937. Calculations from various institutions show the ratio of Paget's disease to all admissions to be from 1:3,000 to 1:16,000. The mono-osteitic type is still rarer, comprising only a very small percentage of all reported. Hurwitz[2] has found that up to the year 1908 there have been only 5 or 6 cases of mono-osteitic type reported in literature in which pathological or x-ray findings have confirmed the clinical diagnosis. Gutman and Kasabach,[1] in an analysis of 116 cases, have found only 6 of the mono-osteitic type.

The following case report is presented here because (1) it is definitely a typical case of a single bone lesion, and (2) because of a number of interesting features in the personal and clinical case-history.

CASE REPORT

Mrs. F.F., Jewish, aged 64 years. On June 1, 1940, she came to my office complaining of a "deformed and forward bowing of the left leg".

Family history.—Her father was of small build, about 4 ft. 5 inches in height, and had been healthy all the time. He died at the age of eighty; the mother also lived to be eighty. She had been slightly taller than the father; she had had no serious illness at any time.

The patient has three brothers. Two brothers are very tall; one is short, about 5 ft. 3 inches. She has five sisters, all of medium height. One sister is very tall—about 5 ft. 11 inches; one sister died at the age of 50, cause unknown. All the other sisters are robust and healthy.

The patient has four sons. They are all tall, three about 6 feet, and one 6 ft. 1 inch.

Past illnesses.—Measles and chicken-pox when a child. In 1926 the patient suffered from a severe cold complicated by otitis media involving right ear. The condition had apparently cleared up completely. She did not think that her hearing had been impaired at all as a result of this attack.

In 1927 she noticed that her breasts were becoming gradually smaller and shrunken. Within a few months a great number of hard nodules appeared in both breasts.

She consulted me in April, 1928. At that time the breasts gave the impression of small bags filled with hard beans. These latter varied in size from a small bean to the size of a walnut. The nodules were freely movable, not tender nor adherent to the skin. The nipples were not retracted. The axillary glands were not enlarged or palpable. The patient was operated upon and both breasts removed in May, 1928.

The removed breasts showed vast cystic changes. Practically all the parenchymatous tissue had undergone cystic degeneration. Some cysts contained thick serosanguineous fluid, others were completely calcified. The diagnosis was undoubtedly chronic cystic disease involving both breasts. The patient made an uneventful recovery.

About 1930 she noticed that she was becoming hard of hearing. The condition had been gradually becoming worse. The ears appeared to be normal.

Present illness.—The patient experienced weakness in left leg, which came on gradually and progressively for about two years. The leg felt too weak to support the body, especially so while climbing up stairs. The weakness was chiefly felt from the knee downwards. There was no pain, but the leg appeared to be getting in the way all the time, and was being bumped against objects quite frequently. She had noticed a slight forward bowing of the left leg about two years ago. About a year ago she was accidentally kicked on the left leg about the middle of the shin. The leg was then painful for a few days only. She thought that after this the bowing of the leg became worse. The bowing was so bad that her friends were beginning to notice the condition and she had to wear long dresses and skirts. By the end of the day the affected leg felt heavy, tired and numb. She was, however, doing practically all her housework unaided.

General physical examination.—The patient was very slim; height 5 ft. 3 inches; weight 111 lbs. She had lost about five pounds in the previous three months. The arteries were not tortuous, only slightly palpable, and did not appear to be sclerosed. The teeth were carious. The tonsils were slightly enlarged. She wore glasses but her vision was not impaired. The pupils reacted normally to light and accommodation; eye grounds, normal. There was no general glandular enlargement. The thyroid was considerably enlarged, the left lobe being a little nodular. The heart, lungs and abdomen appeared to be normal. Reflexes normal.

The skeletal system.—The skeletal system appeared to be normal in every respect, with the only exception that the left tibia bowed forward. The maximum of convexity was a little above the junction of the middle and lower third of the tibia.

MEASUREMENTS

	Right inches	*Left* inches
1. Knee to external malleolus	16¼	17
2. Circumference of calf 8 inches below knee	12	13¼
3. Circumference of ankles above malleoli ..	9	9
4. Circumference of knee	10	10

Radiographic examination.—Skull normal; chest normal. The left clavicle was a little more curved than the right, but showed no evidence of disease (see Fig. 1). Spine normal; pelvis normal; femora normal.

Both legs (tibiæ) were taken at the same time on one plate (see Fig. 2), thus assuring the same exposure on

both sides. Exposures were made in the antero-posterior and lateral positions.

Right tibia and fibula laterally were normal; left fibula normal. The left tibia showed gross pathological changes as follows. Cancellous bone is very much thickened and irregular. The upper part of the bone showed some decalcification and rarefaction. The medullary canal was irregular and very much narrowed in places. There were a great number of areas of softening (small cysts?) in the medullary canal, and also in the anterior part of the cancellous tissue. The fibula was straight and stood out against the bent tibia like a "string in a bow".

Antero-posterior.—The right tibia and fibula were normal (see Fig. 3). The left tibia was considerably wider than the right, irregular and considerably thickened. Density (to x-ray) in the left tibia was much greater than in the right. The density was so great that the medullary canal is only slightly visible in some places. The density in left fibula was also greater than in the right.

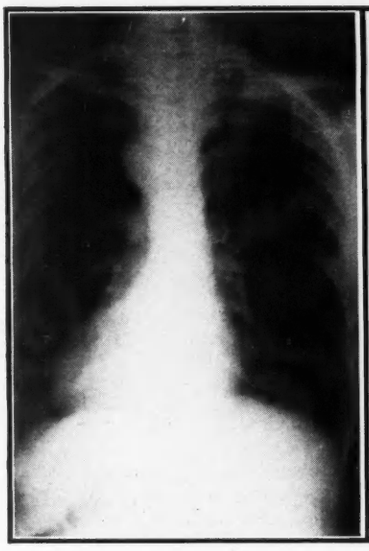

Fig. 1

Fig. 2

Fig. 3

Laboratory tests.—Urine, normal. Red blood cells, 4,200,000; white blood cells, 6,500; hgb. 90 per cent. *Blood chemistry:* urea nitrogen 15.75; creatinine 1.611; sugar 0.116; calcium 11.5; plasma phosphatase 12 Bodanski units; basal metabolism test −5; blood pressure 190/110. Wassermann test negative. The diabetic curve was within normal limits.

COMMENTS

There are a number of interesting points in this case history.

1. Tallness seems to run in this family. All the brothers and sisters are tall, and so are all the sons. This is in conformity with a number of observers who have found that in Paget's disease a history of familial tallness is usually found. It has also been observed that associated with this disease there is usually a familial history of diabetes. Moehlig and Adler,[4] in a series of 26 cases found that 30 per cent gave a familial history of diabetes; 83 per cent a familial history of obesity; and 78 per cent gave a familial history of tallness. Based on these findings, these investigators believe that the underlying cause of Paget's disease can be traced to a lowered carbohydrate tolerance due to pituitary disturbance. So far as can be ascertained there is no diabetes in this patient's family history.

2. Degenerative changes in various organs, resulting in fibrosis and calcification of soft tissues, are very common in people suffering from Paget's disease. In a series of 26 cases studied by Moehlig and Adler[4] and another group of 12 studied by Moehlig and Murphy,[3] it was found that about 40 per cent had adenomatous goitre, of which 15.5 per cent were calcified; 30 per cent of the female patients had uterine fibroids, of which 75 per cent have shown some calcification. Arteriosclerosis is exceedingly common in patients with Paget's disease.

This patient does not show definite signs of arteriosclerosis. However, having a blood pressure of 190/110 suggests the presence of arteriosclerosis somewhere in the system. The patient is suffering from a large adenomatous goitre with nodules that appear to be calcified. I could not demonstrate calcification of the nodules by x-ray. Of particular interest is the finding that the patient had been suffering from a peculiar cystic disease of both breasts in which the entire glandular tissue has become fibrosed and calcified.

3. Impairment of hearing is a common complaint in patient's with Paget's disease, especially when the skull is involved. In a series of 116 cases reported by Gutman and Kasabach[1] 26

complained of deafness. This patient is suffering from a definite and progressive impairment of hearing, although by clinical and roentgenological examinations, involvement of the skull could not be demonstrated. It is not likely that the otitis media from which the patient had been suffering years ago is responsible for the present deafness. Firstly, the otitis media was of a mild origin, which cleared up (apparently) completely in a few days. And, secondly, the otitis media was confined to one side only, while in the present complaint both ears are affected.

4. The absence of pain in this case, in spite of involvement of the whole of the tibia is of great significance. A considerable number of patients with Paget's disease have no other complaint aside from deformity. In these cases it is impossible to determine with any degree of certainty the beginning of the onset of the disease. In the great majority of cases, however, pain is usually the first symptom to appear. Pain, when present, is most distressing and constant and very difficult to control. It is specially common when the pelvis, spine or lower extremities are involved.

5. Blood chemistry examinations are of considerable interest in the study of this condition. The constituents that are most intimately associated with bone metabolism, so far as is known, are calcium, inorganic phosphorus, and phosphatase. The study in a large number of cases has shown that the serum calcium and inorganic phosphorus in Paget's disease are either below or within normal limits. The serum phosphatase is always above normal.

Phosphatase is an enzyme which is normally present in the blood plasma, and possesses the property of hydrolyzing phosphorine esters. The amount of phosphatase in the body is usually expressed in the terms of Bodanski units. The normal level in the blood is 1 to 4 units. An increase in serum phosphatase is found in many conditions of bone lesions where there is an increase in processes leading to new-bone formation, such as carcinoma, etc. The level of serum phosphatase is also increased in the presence of extensive liver lesions. The highest values, however, have been found in Paget's disease. By itself an increase in phosphatase level is of no value in differentiating this disease from any other condition where new-bone formation is taking place. It is, however, of great aid in the diagnosis of the condition when combined with clinical and roentgenological findings.

The extent of bone involvement may be judged roughly from the rate of increase in the serum phosphatase level. In the generalized condition of Paget's disease values ranging as high as 120 to 150 Bodanski units have been found in some cases. In the mono-osteitic type the phosphatase level is usually between 8 to 20 units. In the case under discussion the phosphatase level was found to be 12 units. A low phosphatase level almost always rules out the diagnosis of Paget's disease.

REFERENCES

1. GUTMAN, A. B. AND KASABACH, H.: Paget's disease: analysis of 116 cases, *Am. J. M. Sc.*, 1936, **191**: 361.
2. HURWITZ, S. H.: Osteitis deformans involving a single bone, *Am. J. M. Sc.*, 1914, **147**: 855.
3. MOEHLIG, R. C. AND MURPHY, J. M.: Paget's disease, *Endocrinology*, 1935, **19**: 515.
4. MOEHLIG, R. C. AND ADLER, S.: Carbohydrate metabolism: disturbance in osteoporosis and Paget's disease, *Surg., Gyn. & Obst.*, 1937, **64**: 747.
5. KAY, H. D., SIMPSON, S. L. AND RIDDOCH, G.: Osteitis deformans, *Arch. Int. Med.*, 1934, **53**: 208.
6. NEWTON, F. C.: The mono-osteitic type of Paget's disease of bone, *Arch. Surg.*, 1924, **8**: 24.
7. SUGARBAKER, E. D.: Osteitis deformans, *Am. J. Surg.*, 1940, **48**: 414.

A skin test which tells within less than an hour whether or not a given woman is going to become a mother was announced by Drs. Frederick H. Falls, V. C. Freda and H. H. Cohen, of the University of Illinois College of Medicine. The test is similar to those made for allergy or hayfever. It is said to be 98 per cent reliable. Previously developed tests for early pregnancy take, according to reports of them, from 18 hours to two days. The widely used Ascheim-Zondek test takes two days for a verdict. In the test developed at the University of Illinois, colostrum is used. This is a watery liquid secreted in the breasts during pregnancy until milk formation starts after the baby is born. A tiny amount of this is injected by hypodermic needle into the skin of the forearm. If the woman being tested is pregnant, there is no reaction. If she is not pregnant, a reddish area of one or two inches diameter appears within an hour around the injection point, disappearing within about five hours. Besides the speed and economy of the new test, it is said to be valuable because it helps to differentiate between pregnancy and abdominal tumour and also helps to determine quickly the dangerous condition in which the baby starts developing outside the uterus.—*Science News Letter*, March 22, 1941.

THE USE OF THE NEWER DRUGS*†

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SOME of the drugs of the sulphonamide group have been in use for about five years. During this time success has attended in succession their use in diseases caused by the *B. hæmolytic streptococcus,* the meningococcus, gonococcus, pneumococcus, the majority of urinary tract infections and in staphylococcal infections. These several advances have followed each other so swiftly that sound principles of chemotherapy have become hidden or forgotten in the distraction of ever occurring novelties. Since almost everyone is persuaded that further sudden and even more brilliant advances are shortly to be expected it is desirable at intervals to review the ground that has been traversed.

NOMENCLATURE

One of the serious causes of confusion arises from nomenclature. The parent substance of the sulphonamides, (p.amino-benzene sulphonamide) was discovered by Gelmo in 1908. Since there is no patent protection for this drug it

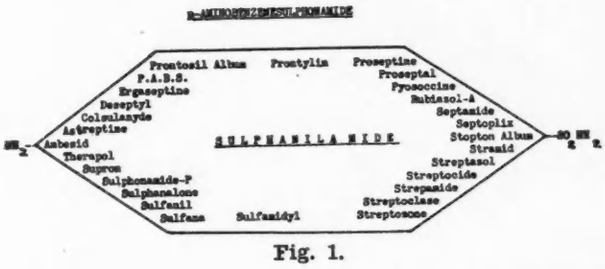


Fig. 1.

would seem only reasonable that one name such as "sulfanilamide" should be used to denote the drug. Fig. 1 indicates how far we are from this happy state.

The "prontosils"‡ which are included in Table I are in one respect the aristocrats of the sulphonamide series. The original prontosil proved the effectiveness of the sulphonamides in streptococcal infection. The prontosils are, unlike sulphonamide, quite inactive *in vitro* and it has yet to be demonstrated that their effectiveness *in vivo* is due to anything but the fact that these compounds are disintegrated in the body to produce sulfanilamide. The sulfanilamide content of these substances is in general about 1/3 of their molecular weight. In other words weight for weight they can at most, in so far as has yet been proved, exert only about the same bacteriostatic efficiency as would be exhibited by 1/3 of the same weight of sulfanilamide. In actual fact, in the human body the elaboration of sulfanilamide from prontosil or neo-prontosil, etc., takes place rather slowly and a great deal of the dyes is excreted intact, staining the urine red. The blood of patients

TABLE I.

THE PRONTOSILS AND OTHER SULFANILAMIDE DERIVATIVES (SULPHONAMIDES), WHICH HAVE BEEN WIDELY USED.

Trade Names	*Remarks*
Prontosil Prontosil rubrum Prontosil flavum Sulphamido-chrysoidin	Solid red dye, not in use in the United States of America and Canada.
Prontosil soluble Prontosil Prontosil-S Prontosil II Neoprontosil Bayer 102 Rubiazol injectable Streptozone-S	A much more soluble red dye in common use in United States of America and Canada, either in liquid or solid form. (For discussion, see text.)
Uleron Uleron (U.S.A.) D.B. 90 D.B. 373 Diseptal A	A disulphonamide of German origin which has fallen into disrepute because of its toxic properties.
Proseptasine Soluseptazine	Benzyl derivatives having most of the disadvantages of the prontosils.
M. and B. 693 (Eng.) Dagenan (Canada) Sulfapyridine (U.S.A.)	Of proven worth (see text).
Sulfamethylthiazole	Withdrawn from clinical tests due to toxicity.
Sulfathiazole	Of proven worth (see text).

* Read at the Seventy-first Annual Meeting of the Canadian Medical Association, Section of Medicine, at Toronto, June, 1940.

† The paper is based on clinical experience in the newer drugs on the Medical Service of the Toronto Western Hospital 1936 to 1940. The clinical observations were made with the collaboration of H. T. Kincey, M.D. The conclusions as to the effect of the drugs on the hæmopoietic system are based on studies made by J. R. Morgan, Capt. R.C.A.M.C. The dagenan was supplied on test by Messrs. Poulenc Frères, Montreal, and the sulfathiazole by Squibbs, of New Brunswick, N.J.

‡ The position of these drugs in therapy may conveniently be dealt with at this point, even if this anticipates the topics which are later to be discussed.

heavily dosed with prontosil very rarely contains as much as 3 mg. of sulfanilamide per 100 c.c. of blood.

From a lack of comprehension of these facts there has arisen a misconception of the effectiveness of the prontosils in fulminating infections which, as would be expected, they often fail to control. It is of course true that even rapidly fatal septicæmias of *B. hæmolytic streptococcal* origin may be caused by strains that are extraordinarily sensitive to sulfanilamide and in these the prontosils have been effective. Since, however, the clinician has no quick way of ascertaining the susceptibility of the bacteriological strain of the streptococcus causing the infection he is on safer ground if he chooses to use adequate dosages of sulfanilamide itself. The usual argument employed to counter this suggestion is that the prontosils are less toxic than sulfanilamide. This half truth, which has received very wide acceptance among practising physicians, also springs from a lack of understanding of the facts already mentioned. If it were certain that the elements in the large prontosil molecule were completely devoid of any toxic action—and this is doubtful—the only toxic action of the prontosils would be due to the sulfanilamide freed by the breakdown of the azotised (prontosil) molecule in the body. On a weight for weight basis we have noted that at the most this could not exceed 1/3 and in actual practice is probably closer to 1/6 or 1/5 of the total amount of prontosil absorbed into the blood stream. It would, under these circumstances, be a much fairer test to compare the toxicity of doses of at least three times as much prontosil to that of sulfanilamide. It is also worth mentioning that prontosil, neoprontosil, etc., stain the blood and tissue fluids red. This effectually masks cyanosis which, as is now recognized, is more alarming to the physician and friends than it is dangerous to the patient. It is unfortunate that it has too often and wrongly been interpreted as a reason for discontinuing chemotherapy.

The prontosils are safe, but not for the reasons usually advanced. They are often ineffectual in very severe infections for the reasons given. Their value is in dealing with infections sensitive to small doses of sulfanilamide, particularly those not immediately dangerous to life and in which delay in producing a cure is not of serious import. It is our opinion that for use against potentially lethal infections there are much better drugs available.

For the reasons given the prontosils have confused the minds of many as to the effectiveness of chemotherapy. To the misconceptions fostering such confusion must be added the unnecessary confusion which emanates from the nomenclature (Table I). In Germany, where the original patents of the prontosils are held, the views expressed above would be denounced as heretical; but then in Germany sulfanilamide (rediscovered by the French) is looked upon unfavourably.

Sulfapyridine, mercifully, has not yet become an obsession among those who have a flair for devising synonyms. It is known in England as "M. & B. 693"; in Canada as "dagenan" (a corruption of Dagenham where it is manufactured), and in the United States as "sulfapyridine". It is conceded that it is quite effective against the organisms susceptible to sulfanilamide and has in addition the power of inhibiting the growth of the pneumococcus.

Sulfathiazole has now emerged from extensive clinical trials. It has the valency of sulfapyridine with an added power of combating infections caused by some strains of the staphylococcus aureus.

Mode of Action

While it is true that the empirical work of earlier investigators was supported by animal experimentations and that the contributions of Domagk, Colebrook, Nitti, Long, Marshall and their collaborators,—to mention only a few—provided a sound basis for safe treatment and clinical research, yet the key essential to a complete understanding of chemotherapy has remained elusive. Most observers have agreed that the action of sulfanilamide was one of growth inhibition or bacteriostasis, but how or why bacteriostasis was brought about was not known. Some measure of success has lately seemed to reward the efforts of the numerous workers engaged in the search for the mode of action of the sulphonamides. In a recent article Fildes, reviewing the researches initiated by Lockwood and pursued by McIntosh, Fleming, Whitby, Stmp, Green, Woods, Selbie and Fildes, states that the results are "in agreement" in ascribing the action (of sulfanila-

mide) to interference with bacterial enzymes associated in some way with nutritive substances''. In other words, sulfanilamide starves *hæmolytic streptococci* by blockading them from an essential food. Woods has shown that *in vitro* para-aminobenzene sulphonamide (sulfanilamide) apparently causes bacteriostasis of the streptococcus by interfering in the ultilization by the latter of a substance (para-aminobenzoic acid) which is supposedly essential to the growth and multiplication of the streptococcus. Selbie has advanced evidence that the same is true *in vivo* for mice. This interference, it is suggested, is effected by the seizure by sulfanilamide of an enzyme system which is the necessary vehicle in making para-aminobenzoic acid utilizable by the *hæmolytic streptococcus*. It is further suggested that competition for the enzyme system by these two substances is made possible by their similarity of structure and that *such competition obeys quantitative laws.*

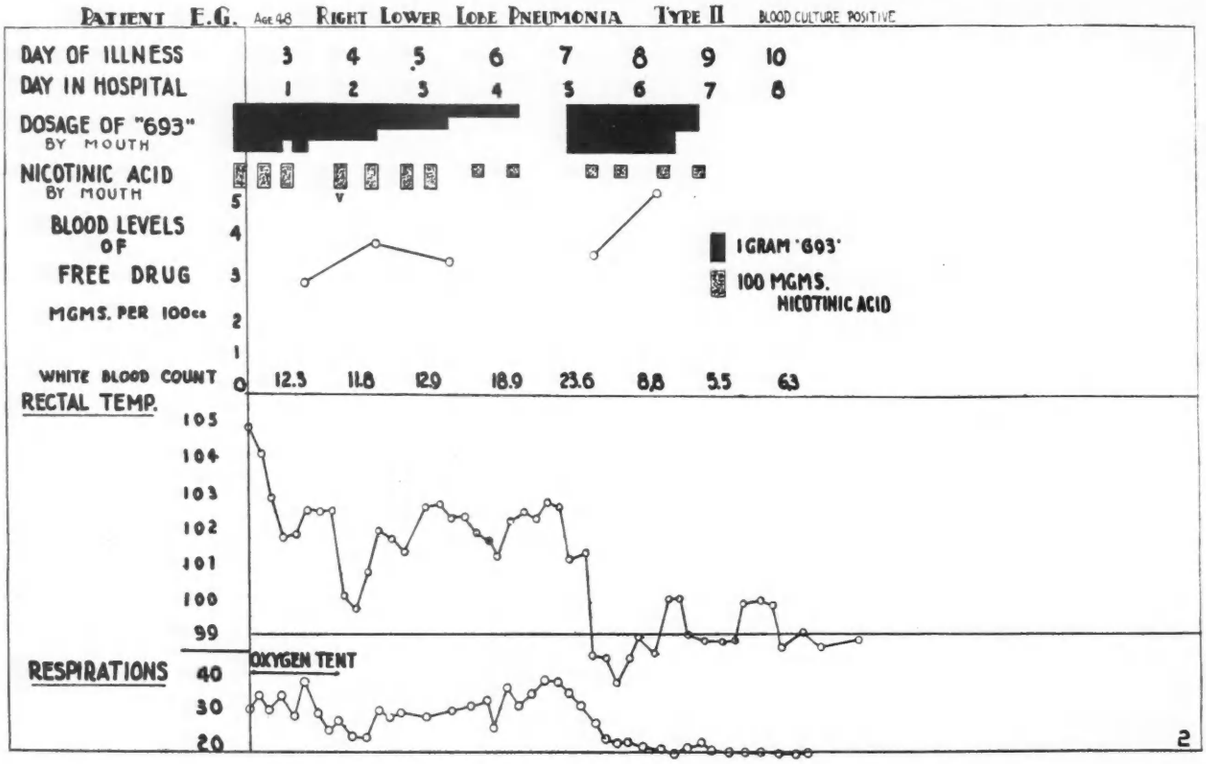
The conception of a quantitative competition for a single vehicle would serve to explain, in part at least, a number of hitherto imperfectly understood features of the action of sulfanilamide both in the laboratory and in clinical medicine. For example both in cultures and in patients there is a lag period of 5 to 6 hours before the bacteriostatic effect of sulfanilamide becomes manifest. This may be attributed to the time required for the blockade to produce the telling results of deprivation. Further, the action of certain substances such as peptone (Lockwood), which have been demonstrated to inhibit the bacteriostatic action of sulfanilamide in cultures and which contain para-aminobenzoic acid becomes explicable.

A wide clinical application of the above mentioned theories is not yet justifiable, but it is perhaps permissible to browse on the edge of the field of speculation. For example it is obvious, assuming the validity of Filde's views, that organisms not dependent upon a particular enzyme system for the utilization of para-aminobenzoic acid, or those which are less dependent upon this metabolite will not easily be susceptible to sulfanilamide. If it can be shown that it is only through this restricted channel (and there are of course other theories) that sulfanilamide exerts its bacteriostatic effect then diseases caused by bacteria which are immune to this form of attack are quite unsuitable for sulfanilamide therapy. We are doubtless on the verge of a great many discoveries in the field of what might be termed nutritional or biochemical bacteriology which will finally dictate our selection of chemo-therapeutic weapons against human disease. Secondly the ''quantitative competition'' hypothesis provides cogent support for early and adequate dosage in chemotherapy. The blockade aimed at producing starvation of the streptoocccus should be fully operative at the earliest possible moment. In fulminant cases the first dose should be large enough to achieve this object. Thirdly, since streptococci themselves have been demonstrated to contain para-aminobenzoic acid it is probable that pus containing the dead streptococci and tissue débris is also rich in this substance so that the failure of sulfanilamide in the treatment of closed abscesses is clarified.

Fildes has drawn attention to the cousinship in molecular structure of sulfapyridine and nicotinic-acid or vitamin B_2 (pyridine ring). As in the case of sulfathiazole there is as yet no published work to support the purely hypothetical suggestion that sulfapyridine acts to blockade the utilization of the essential metabolite, nicotinic acid, from bacteria and from the cells of the host. The idea rests only on the expectation ''that the antibacterial substance should have a chemical similarity to the essential metabolite''. If, however, it should be proved that sulfapyridine interfered with nicotinic acid utilization there would be grounds for believing that the administration of nicotinic acid might, on the quantitative competition hypothesis, act as an antidote to sulfapyridine. Such highly speculative theorizing would have no legitimate place in a paper of this character were it not the case that some pharmaceutical firms are producing tablets containing sulfapyridine associated with nicotinic acid. Until the position becomes much clearer than it is at present it would seem wiser to await the result of further research.

About one year ago at the writer's suggestion we administered nicotinic acid in doses of 200 mg. per day to 21 cases of pneumonia which were receiving intensive sulfapyridine therapy. We did this in the hope that nicotinic acid might diminish the incidence of vomiting. A decrease in the frequency and severity of vomiting was sometimes apparent but we discontinued the practice because it was noticed that in two cases there seemed to be an unsatis-

factory response to sulfapyridine when nicotinic acid was given (Fig. 2). Since Fildes' paper appeared these cases have been again reviewed. In 19 cases the level of sulfapyridine in the blood was over 8 mg. per 100 c.c. In other words these cases fell into a group which were being treated on a very intensive dosage. In none of these cases was there any indication that the administration of nicotinic acid in any way modified the effective action of sulfapyridine. The remaining two cases failed to absorb the drug well (levels in the blood were not higher than 5 mg. per 100 c.c.) and in both there was some evidence of inhibition of sulfa-


PATIENT E.G. Age 48 RIGHT LOWER LOBE PNEUMONIA TYPE II BLOOD CULTURE POSITIVE
DAY OF ILLNESS
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BLOOD LEVELS OF FREE DRUG MGMS. PER 100cc
1 GRAM '693'
100 MGMS. NICOTINIC ACID
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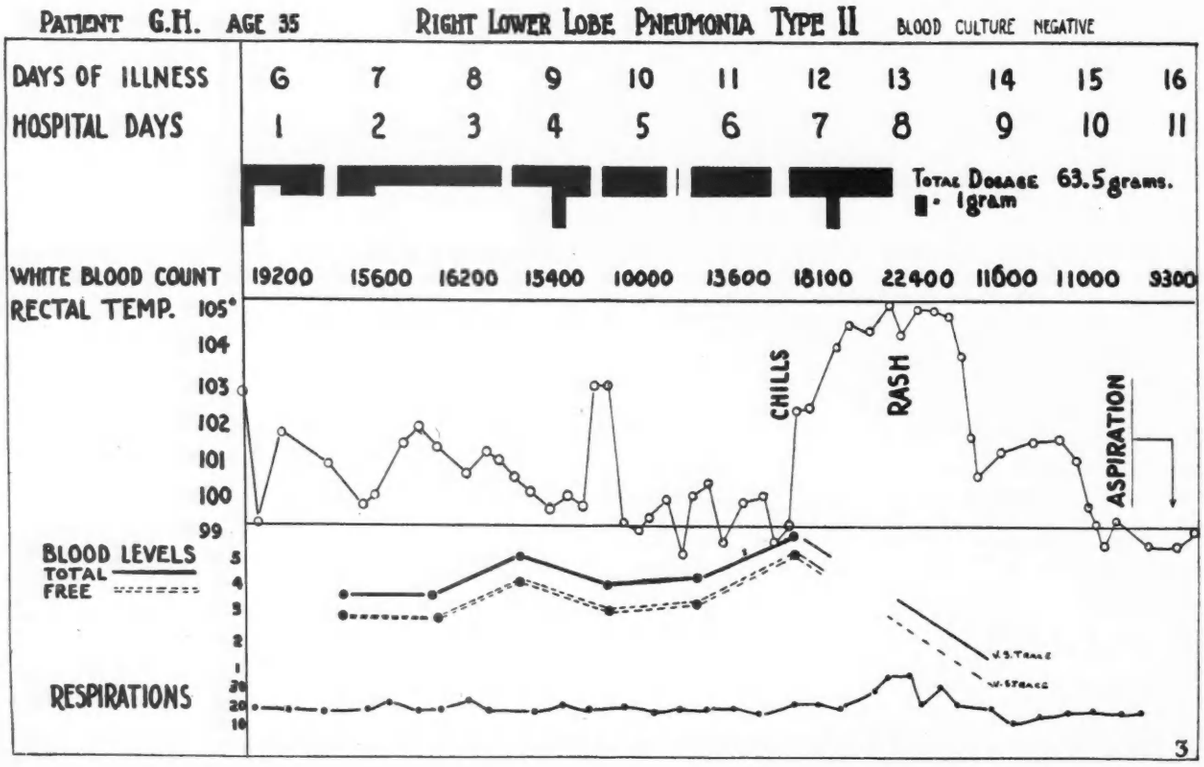

pyridine effectiveness (Fig. 2). It is, however, noteworthy that one case while receiving heavy dosage along with 25 mg. of nicotinic acid with each dose developed a drug rash and drug fever. These results are quite inconclusive but they suggest that nicotinic acid should not at present be given with sulfapyridine because it possibly may interfere with effective action of the latter upon bacteria.

THE PRINCIPLES GOVERNING THE USE OF CHEMOTHERAPY

The discoveries reviewed by Fildes, however unready in detail for application at the bedside, may provide a rational working basis for the clinical use of the newer drugs. Certain broad principles which were already known or were being recognized have by this work received timely and substantial support.

In earlier papers it was not infrequently emphasized that the most dramatic cures occurred in the most acute infections. Septicæmia due to meningococci or streptococci were often quickly arrested by adequate chemotherapy, whereas chronic infections with abscess formation were notoriously difficult to combat. All physicians are able to differentiate the invasive phase from the chronic or entrenched stage of a disease. The necessity for so doing is of prime importance. It is in the invasive stage (Table II) that chemotherapy is of most value. From Fildes' review it can be appreciated why this is so. If we visualize the onset of a streptococcal infection as an invasion effected by organisms whose hope of conquest lies in their power to multiply a million fold on the battlefield itself, then it is clear that they are most vulnerable when they are living off the country; while they are forced to forage. During the invasive stage they are seizing the food designated for the defender and if at one blow this can be denied them their power of multiplying is gone and it remains only for the defender to mobilize his forces, totally to exterminate them. This sudden blockade can, we have seen, be instituted by the newer drugs. If on the other hand the starvation tactics are not used, or used only in half measures, it is possible that the invaders become numerous enough to get a footing from which they cannot be dislodged by an attempt at starvation. We have seen that in this stage streptococci, for example, soon have enormous supplies of essential food stuff by the production of pus and with this secured the earlier effectiveness of the chemotherapeutic weapon (quantitative competition) becomes relatively powerless and its continued employment may soon become a greater menace to the patient, whose tissues also require the essential metabolites, than to the entrenched organisms.

In the invasive stage then the slogan should be "hit quickly, hit hard and keep on hitting". "Hit quickly" because the bacteria are multiplying at an enormous rate and threaten to overwhelm the defenses of the body. "Hit hard" because if maximum benefit is to follow therapy enough of the drug must be present successfully to compete, in a quantitative way, for the sources of supply. "Keep on hitting" because too rapid withdrawal of the drug may find the defenses of the body still imperfectly mobilized.* When this is the case exacerbation of the acute phase may occur, followed by what is worse, the destruction of the integrity of the

* Except in meningitis it is seldom wise or necessary in acute infections to continue chemotherapy longer than 8 days.

Fig. 2.—Illustrating the clinical course of a patient who received dagenan and nicotinic acid concurrently. Bacteriostatic tests showed that the particular pneumococcus was very susceptible to dagenan *in vitro;* inhibition of growth being complete in the presence of three and five mg. of dagenan per 100 c.c. There was an initial improvement of the patient corresponding with the use of oxygen, dagenan and nicotinic acid, but the fourth dose of nicotinic acid was not retained (indicated by "V"=vomited, in the chart). The crisis occurred on the 7th day of disease and coincided with increased administration of dagenan with the attainment of higher blood concentrations and a reduction in the amount of nicotinic acid being given. The probability is strong that a natural crisis occurred at this time. The suggestion is that something (nicotinic acid) interfered with action of dagenan in this patient in the earlier days of chemotherapy. **Fig. 3.**—The clinical progress of a case of pneumonia treated by sulfathiazole until drug intoxication became grossly evident as shown by chills, dyspnœa, fever, leucocytosis, tachycardia (130 per minute), the appearance of conjunctivitis and a drug rash. On the 8th day of treatment copious diuresis following the administration of over 4,000 c.c. of fluids (2,000 c.c. of intravenous 5 per cent glucose saline). The urinary output rose to 4 litres and over 10 grams of sulfathiazole was excreted in 48 hours (8th and 9th hospital days). The rash lasted three days. The chest was aspirated on the 11th day in hospital and 100 c.c. of sterile straw coloured fluid was withdrawn. The patient made an uneventful but slow recovery. Signs of delayed resolution persisted until the 40th hospital day but the illness ran an afebrile course after the 10th day in hospital.

tissues, and the establishment, with collections of pus, of a subacute or chronic stage.

It has been insufficiently realized that the use of chemotherapy in the chronic stages of infections requires a different technique from that employed in the acute cases. Here massive doses are seldom justified. If moderate doses are not quickly effective continued dosage is unlikely to lead to anything but drug intoxication of the patient. It is important to realize in both acute and chronic stages of infections that if a decisively beneficial result is not obtained within 48 to 72 hours with an adequate amount of the drug, either chemotherapy will fail, the organism being insensitive to this form of attack, or additional measures are necessary. It cannot be emphasized too strongly that chemotherapy has in no way altered an old surgical dictum "where there is pus let it out". Today there is less danger in pus-letting if an effective drug is used before, during and for a few days after the operation. It may prevent a further and disastrous spread of the infection and constitutes no complication of the necessary anæsthetic procedures. On the other hand, long continued dosage by the newer drugs with delay in surgical drainage is not only useless but positively dangerous.

It should never be forgotten in these days of enthusiasm for the newer drugs that the human body has potentially great powers of defence against infections. These defences require time for their elaboration. Very virulent infections are rapidly lethal because the onset of the attack is carried out at a tempo which overwhelms the defences before they can be organized. The newer drugs, effectually used, are capable of holding the invaders in check until the "immunity mechanism" of the patient is in a state to fight them off. In the final analysis it is the antibodies themselves and not the chemotherapeutic agents which exterminate the invading

TABLE II.

EFFECTIVENESS OF THE NEWER DRUGS IN TREATMENT

Drugs	*Stage of disease*	*Organism*	*Clinical diagnosis*	*Effectiveness*
Sulfanilamide Sulfapyridine Sulfathiazole	Invasive or before the purulent lesions develop.	*B. Hæmolytic streptococci.* Meningococci. Gonococci. *E. coli.*	Early middle ear infections and mastoiditis. Cellulitis. Erysipelas. Puerperal sepsis. Septicæmia. Urethritis and arthritis. Pyelitis, Cystitis.	Curative. (Sulfanilamide is usually the drug of choice.)
		Other urinary infectors excepting enterococcus fæcalis.	Pyelitis, Cystitis.	Fairly satisfactory. (Especially sulfathiazole which also has some action on streptococcus fæcalis.)
Sulfapyridine Sulfathiazole	Invasive or before abscess formation.	Pneumococci.	Pneumonia.	Curative.
Sulfapyridine Sulfanilamide	Invasive.	Streptococci. Meningococci.	Meningitis.	Curative in heavy dosage. (Serum advisable as well with meningococci.)
Sulfapyridine	Invasive.	Pneumococci.	Meningitis.	Curative in heavy dosage. (Serum advisable as well with meningococci.)
Sulfathiazole	Invasive before purulent lesions develop.	Staphylococcus aureus.	Septicæmia. Cellulitis.	Curative for some strains.
Sulfanilamide Sulfapyridine Sulfathiazole	Chronic stages with purulent lesions.	Any of the above.	Any of the above.	Poor or nil. (Surgery is required when possible.)

Chemotherapy is worth a short trial in the following diseases with some hope of its being effective:

Staphylococcic infections	Brucellosis	Typhoid fever
C. Welchii infections	Ulcerative colitis	Plague
Friedlander's bacillus infections	Venereal lymphogranuloma	Ulcerative endocarditis
H. Influenzæ meningitis	Scarlet fever	Streptococcus viridans endocarditis

Chemotherapy alone is scarcely worth a trial or is of no value in the following:

All abscesses (empyemata, etc.)	Rickettsial diseases	Infectious mononucleosis
Tuberculosis	Rheumatic fever	Malaria
Virus diseases	Rheumatoid arthritis	Spirochætal infections
Typhoid fever		Fungus infections.

bacteria. Disregard of this profoundly important fact implies a misunderstanding of the proper employment of the newer drugs, and has led to widespread abuses. The time probably will come when tests revealing the degree of mobilization of the biological defensive system *vis a vis* the particular infecting organism will be used to indicate when chemotherapy may be safely discontinued.

Other considerations bearing on this aspect of the problem also deserve notice. In our opinion to deny a patient, seriously ill with pneumonia, adequate anti-pneumonia serum when sulfapyridine or sulfathiazole are not being decisively effective is worse than evidence of poor judgment. We also make it a rule that patients whose blood contains less than 55 per cent of hæmoglobin must have blood transfusions in addition to whatever chemotherapy is being employed. There has been some suggestive evidence that the sulphonamides may in some way alter the characteristics of the recipient's blood so as to render blood groupings more uncertain and thus increase the danger of transfusion reactions. We have on four occasions witnessed unexpected and severe reactions to transfusions with what appeared to be compatible blood but we are not yet prepared to admit that we believe them to have been entirely due to the action of a sulphonamide derivative.

DOSAGE

The common indications for the selection and use of sulfanilamide, sulfapyridine and sulfathiazole are shown in Table II. It remains to discuss the amounts of the various drugs which should be used. In severe infections endangering life, such as septicæmia, meningitis, gas gangrene and pneumonia it is imperative that the appropriate drug should be employed at once in massive doses. When confronted with such a problem we must depend initially upon our knowledge of pathology and on our clinical observations. The use of the swab or blood culture must not be omitted before treatment is begun. The report on the cultures usually will be available in from 24 to 72 hours and if by that time no favourable response has been achieved with the particular drug in use a change should be made to a more appropriate drug (Table II) or to an alternative treatment. Incidentally, I have never seen any harm arise from following one drug with another unless signs of drug poisoning were already manifest.

The dosage for very severe infections, such as those under consideration, should be designed to raise the blood concentration to between 10 to 15 mg. per 100 c.c. of blood as soon as possible in the case of sulfanilamide, and to between 4 and 7 mg. per 100 c.c. in the cases of sulfapyridine or sulfathiazole. With sulfanilamide this can be done by giving ½ grain for every pound of body weight in the first dose.* A man of 150 lbs. in weight should receive 75 grains in the first dose along with 20 grains of sodium bicarbonate. About one-fourth of the initial dose should then be given every 4 hours with 10 grains of sodium bicarbonate during the acute stage of the illness. As soon as marked improvement has become manifest—and this should happen within 48 hours—the maintenance dose should be reduced at first *by* one-third and later *to* one-third every four to six hours. The drug should be continued in small doses until obvious signs of active infection have disappeared.

After a good deal of trial and error we have adopted the following schema of dosage for adults in the use of sulfapyridine and sulfathiazole in the treatment of pneumonia. The initial dose should be large because it is unlikely that it will cause immediate vomiting and it is essential to raise the blood levels to the optimal levels at once. Three to 4 grams (45 to 60 grains) should be given in the first dose and maintenance doses of 1 gram (15 grains) to 1.5 grams every four hours should follow for the next 48 to 72 hours after which some modification is desirable. Pneumonia patients seldom require such treatment for longer than 6 to 7 days unless complications (empyema, etc.) are present. Persistence of fever and illness should always stimulate a search for such complications. It should be remembered however, that fever, sometimes with a rash, is not infrequently due to drug intoxication.

In cases of pneumococcal meningitis or staphylococcal septicæmia the initial doses of sulfapyridine or sulfathiazole respectively should follow that outlined for sulfanilamide; the infection being so dangerous as to warrant the strongest possible attack. It is important to recognize that sulfathiazole does not easily pass over into the cerebrospinal fluid and is therefore quite unsuitable in cases of meningitis.

* In the very obese the ideal weight should be taken as there is evidence that fat does not take up as much of the drug as does useful tissue.

INTRAVENOUS THERAPY

In the event that the drugs cannot be given by mouth or when analysis of the blood shows that despite adequate oral dosage the absorption has been insufficient it is necessary to fall back on injection methods. Sulfanilamide is soluble in about one part in 100 in saline or suitably buffered solutions (1/6 N sodium lactate). A 0.8 per cent solution is thus easily prepared by bringing the sterile solvent to a boil for a few minutes and after removing from the flame adding the appropriate amount of crystalline sulfanilamide. In one case (gas gangrene) the writer has injected 6 grams in a single dose intravenously without any ill effect. If need be such solutions of sulfanilamide may be injected subcutaneously.

Sulfapyridine and sulfathiazole are so very insoluble at body heat that the sodium salts must be used for intravenous or intramuscular therapy. These are very soluble in distilled water and should not be used intravenously in strengths higher than 5 per cent, and should be injected slowly. They are both strongly alkaline and on this account should not be given subcutaneously.

DOSAGE IN MILDER INFECTIONS

Infections which are chronic or semi-chronic or those which are of low virulence are frequently disappointing in their response to chemotherapy, (excepting those causing urogenital disease). In such infections the doses advocated above may be cut in half. Even in these reduced amounts it must be stressed that prolonged treatment without distinct evidence of improvement is dangerous. Clinical trials of chemotherapy in such infections in the absence of suitable bacteriological evidence are sometimes unavoidable but such trials should be tentative and of short duration. It is less dangerous to give a short course of 48 to 72 hours of intensive therapy than to continue with small doses for over 10 to 15 days.

THE LOCAL APPLICATION OF THE NEWER DRUGS

Reports of an encouraging but tentative character have appeared in both surgical and dental periodicals on the topical use of sulfanilamide, sulfapyridine and sulfathiazole in locally infected areas. Experience in the treatment of empyemata by injecting soludagenan (sodium sulfapyridine) into the pleural cavity has yielded disappointing results and this failure has served to emphasize the necessity for surgical drainage in such cases. Three and one-half years ago we tried treating moribund cases of generalized peritonitis by multiple intraperitoneal injections of 0.8 per cent sulfanilamide in saline but the results were poor. On the other hand the introduction of 3 to 5 grams of the powdered (pure) crystals of sulfapyridine or sulfathiazole through an incision into the peritoneal cavity in cases of generalized peritonitis following the rupture of an appendix or a duodenal ulcer has in our experience yielded excellent and very encouraging results. Such procedures are still in the experimental stage and should be carried out with due regard to the possible generalized toxic reactions which may follow them.

THE TOXIC MANIFESTATIONS OF THE NEWER DRUGS

The newer drugs are toxic. They may, while being used to thwart a fatal outcome, be themselves the cause of death. They are occasionally dangerous even in moderate doses for some individuals. These facts are not to be denied. The same is true of a large number of drugs which are in every day use; but with these long experience has enabled us to evolve safe rules governing usage. On the other hand improper evaluation of the toxic reactions of drugs often has led the cautious physician to deny the patient the full benefit of therapy. Between the limits of careless abandon and excessive timidity lies the province of success without tears.

MILD TOXIC REACTIONS

There are certain toxic manifestations of the newer drugs which, even in moderate severity, are not contraindications to the continuation of chemotherapy. Into the category of mild toxic reactions fall the following: headache, anorexia, nausea, vomiting, cyanosis, dizziness, depression, somnolence, ringing in the ears, blurring of the vision, monotony of speech and diarrhœa. Of these, with sulfanilamide, headache, cyanosis and dizziness are very common, whereas nausea, anorexia, vomiting and depression are much more common with sulfapyridine. Sulfathiazole gives rise less frequently to nausea and vomiting than sulfapyridine and very seldom, if ever, causes cyanosis.

Vomiting caused by sulfapyridine can be very severe and exhausting. It may thus militate against recovery both by its effect on the patient and the barrier it may erect against continued treatment. Although it is apparently of central origin yet there is evidence that local irritation may play a part in its causation. Because of this the administration of 1 gram of the powdered tablets in 1 drachm of ½ B.P. strength of fresh mucilage of tragacanth often reduces the severity of this complication or prevents it altogether.

Cyanosis, as has been said, is a much exaggerated cause for alarm during treatment by sulfanilamide. Earlier it was considered likely that much of the cyanosis was due to sulphæmoglobinæmia. This view has now been abandoned and with it have gone the many dietary restrictions (onions, eggs, sulphates, etc.) which were once imposed. The cyanosis is usually due to either methæmoglobinæmia, or to a breakdown product of the sulphonamides or to both together.

Dizziness.—It is important to limit the activities of people who are taking sulphonamide derivatives. They should not be permitted to operate machines requiring precise manipulation or judgment. They should never drive automotive vehicles.

REACTIONS OF MODERATE SEVERITY

Next to be considered are those toxic reactions which although by themselves not necessarily fatal may nevertheless be either the precursors of more dangerous sequelæ, or if neglected may cause progressive and grave deterioration of the condition of the patient. As soon as these side-effects become apparent, treatment should at least be interrupted if not terminated altogether.

Nervous twitching.—Convulsive movements of localized muscle groups sometimes becoming multiple are occasionally seen when the concentration of sulfapyridine in the blood rises to high levels.

Delirium.—It is not generally recognized that mental disturbance amounting to mania which lasting for days and occasionally for weeks or months may be caused by intoxication by the newer drugs. In our experience this has been most frequently seen when sulfapyridine has been used.

Peripheral neuritis is a rare complication which in our experience has been observed with both sulfapyridine and sulfanilamide. Its frequent occurrence marred the otherwise considerable promise of the drug "Uleron" and was the reason for the withdrawal of sulfamethylthiazole during the progress of clinical trials.

Acidosis.—Because the administration of sulfanilamide is accompanied by a considerable loss through the kidneys of bases (*e.g.*, sodium) there is a distinct danger of acidosis occurring. Sodium bicarbonate is therefore always given with sulfanilamide. This is not the case with either sulfapyridine or sulfathiazole.

Rashes and fevers.—All three of the drugs under consideration may cause pyrexia and cutaneous erruptions. These usually occur from the sixth to the ninth day, seldom before the fourth day but have been observed during the first few hours of chemotherapy. Patients who have previously exhibited drug rashes and fevers while receiving sulphonamide derivatives usually show similar and often earlier and more severe reactions on readministration of such drugs. As a general rule, to which there are exceptions, rashes usually follow a variable period of drug fever. They are always signs of drug intoxication and are rightly considered as justification for the immediate termination of chemotherapy. The rashes of sulfanilamide and sulfapyridine are usually macular or maculo-papular, sometimes scarlatiniform and rarely exfoliative in character. Unless the drug intoxication is very severe the conjunctivæ escape. Exposure to sunlight is a predisposing factor in their appearance. They occur in from 6 to 8 per cent of cases.

Sulfathiazole is particularly likely to produce rashes of a type resembling erythema nodosum or urticaria although both scarlatiniform and macular rashes have been observed. The pseudo-urticarial or erythema-nodosum type of rash commonly appears on the forehead and malar regions, on the forearms and hands, shins and feet and is very frequently accompanied by a conjunctival infection or even hæmorrhage. When very severe the mucous membrane of the lips, mouth and throat may erupt and become painful.

The occurrence of a drug fever during the treatment of a febrile illness is often extremely difficult to detect. It used to be thought that these drug fevers were unaccompanied by either chills or leucocytosis but as clinical ex-

perience has been accumulated this view has had to be modified. Especially in the case of sulfathiazole, but also true of sulfapyridine, fever swinging to 103 or 105° not infrequently accompanied by chills and a marked leucocytosis (as high as 35 to 40,000 has been observed) is not at all unusual in severe drug fevers. More usually the leucocytosis is only moderate and chills are absent. The appearance of a rash is of course a tell-tale indication of the true state of affairs but as this is frequently late in occurrence the clinician may be placed in a very difficult position. The writer has noticed that at the height of a drug rash it is common to find râles and sometimes altered breath sounds at the bases of the lungs. I have also made the mistake of believing that the increased fever, pulse and respiratory rates, leucocytosis and spread of minimal signs in the lungs were indications of an extension of an infective pneumonia and have recognized the error only when the rash appeared (Fig. 3). Such patients are on the basis of the physical signs unaccountably very ill. After the fourth day of chemotherapy, if a thorough physical examination fails to provide a reasonable basis for either a continuing fever or an unexpected rise in temperature and leucocytosis, it is always wise to interrupt chemical treatment and see what then occurs. When treatment is interrupted by reason of toxic manifestations the fluid intake should always be augmented in an attempt to remove the drug from the body as soon as possible.

Hepatitis.—There is reason to believe that the sulphonamide drugs may cause hepatic damage. The appearance of jaundice during chemotherapy is usually considered as an indication for the discontinuance of treatment. On the other hand cases having jaundice beforehand have been successfully and, apparently, safely treated by these drugs.

THE GRAVER TOXIC MANIFESTATIONS

There are only two important toxic effects of the newer drugs which have been known to cause death. These are damage to the urinary organs and tract and damage to the formation or the integrity of the cellular elements of the blood.

Renal irritation and anuria.—The urinary complications of chemotherapy arise chiefly from supersaturation of the urine by the conjugated or acetylated compounds of the several drugs. There is in addition the probability that high blood concentrations of the drugs even in the free or unconjugated form may cause a toxic degeneration of the renal epithelium, especially when such high blood concentrations are the result of urinary retention. Sulfanilamide and sulfathiazole in the absence of renal retention are not rapidly acetylated or conjugated in the body. The more insoluble acetylated forms of the drugs are therefore not present in large amounts and hence are less likely to be excreted under conditions of supersaturation in the urine. With sulfanilamide very few instances of this occurring have been reported since owing to its greater solubility acetylsulfanilamide seldom crystallizes out in the urine. Acetyl sulfathiazole is the most insoluble of all the drugs under consideration, and its crystals are often present in the urine. It is therefore a potential, although apparently to date, a seldom incriminated source of trouble. Possibly it owes some of its immunity from bad report to the fact that the experience with sulfapyridine has led to its more cautious clinical use.

Sulfapyridine is not only acetylated very rapidly but is also excreted more slowly than either sulfanilamide or sulfathiazole by most patients. The acetylated form of the drug is very insoluble and precipitates as small flat lancet-shaped crystals which may possibly irritate the renal tissues and cause gross hæmaturia. The crystals may clump together in the tubules or more frequently in the renal pelves and ureters and cause obstruction and oliguria or even anuria which may be accompanied by pain in the loins. The administration of alkalis does not lessen this danger and the only effective preventive measure is the maintenance of a urinary flow of greater than 1,000 c.c. in 24 hours. Fluid restriction during treatment with sulfapyridine is fraught with danger and this is increased by the vomiting which is induced by the drug. The fluid intake should not fall below 3,000 c.c. in 24 hours. Since there is some evidence that sulfapyridine may cause a toxic nephritis, cases which have been rendered anuric are properly treated at first by intravenous injections of 300 to 400 c.c. of hypertonic glucose solution (25 to 50 per cent). If no relief from the anuria is obtained by this means within 12 hours recourse should be had to a cystoscopic introduction of ureteric catheters into the plugged ureters and lavage of these channels by sterile water.

Toxic effects on the Red Blood Cells.—Sudden severe acute anæmia accompanied by hæmolytic jaundice may occur at any time during treatment by sulfanilamide. The other two drugs are much less culpable in this regard although all may cause anæmia of gradual onset. Death is usually easily avoided by the alert physician with the immediate cessation of chemotherapy and transfusions.

Toxic effects on white cell production.—Although all three drugs may cause a rapid decrease in the production of the polymorphonuclear elements the culpability falls in the order of sulfapyridine, sulfanilamide and sulfathiazole. Long-continued treatment (over 10 days) with even moderate dosage of sulfapyridine is particularly likely to cause agranulocytosis which may occur without 24 hours' warning. When the white cell count falls to 5,000 cells per c.mm. a very careful watch must be kept on the differential count. Should the proportion of the polymorphonuclear cells begin to fall toward 50 per cent of the total count the signal has been given to discontinue chemical treatment and administer fluids to free the body of the drug. Some cases of complete agranulocytosis recover spontaneously but in the majority of instances no treatment is of avail in thwarting the fatal outcome. Leukopenia of milder character is also more commonly a complication of sulfapyridine than of sulfanilamide and sulfathiazole.

By way of summary it may be said that sulfanilamide is still the best drug against the infections in which long experience has proved its usefulness. It may be that sulfathiazole will displace it from this position but until this drug has received further trial sulfanilamide should retain its old place both by reason of its effectiveness and the clear recognition of its toxic properties. Sulfapyridine in our experience has the same valency, somewhat more potent in some instances, as sulfanilamide and in addition is very effective against pneumococcal infections. Its chief disadvantage in use lies in its very toxic properties. This is by no means confined to nausea and vomiting but extends to its very serious urinary complications and a greater general toxicity, including the hæmopoietic system. Sulfathiazole has a very effective action within the valencies of both sulfanilamide and sulfapyridine as well as being more potent in some staphylococcal infections. Against pneumococcal infections although quite effective it is usually not as dramatic in action as is sulfapyridine, there apparently being a longer "lag" period and therefore a less rapid fall in temperature. It is not of value in meningitis and occasionally fails to control pneumonia in which sulfapyridine is later found to be effective. It is apparently much less toxic than sulfapyridine but should be used with the same caution which is necessary when giving any of the sulphonamides. Restriction of the fluid intake is dangerous when either sulfapyridine or sulfathiazole are used.

In the use of all three drugs short intensive dosage is less dangerous than long-continued chemotherapy with small doses. When used to combat potentially lethal infections these drugs should be given in heavy initial doses and entirely withdrawn if they are ineffective after 48 to 60 hours. Constant vigilance is necessary to guard against the occurrence of the severer toxic reactions. Estimations of the hæmoglobin and the white blood count should be made frequently and a careful watch kept on urinary output.

Since the introduction of aspirin forty-one years ago by Dreser, many reports have appeared on the adverse effects which may follow its unwise use. These have included depression of the heart, habit formation, miscarriage in pregnancy, and idiosyncrasy causing such alarming symptoms as urticaria (hives), pruritus (itching), erythema (redness of skin) and generalized angioneurotic œdema (swelling of the skin due to a blood vessel disorder). Cutaneous (skin) eruptions of various forms are not unknown, and even ulceration and gangrene have been attributed to its use. Because of the irritant action of the products containing the salicyl group on renal epithelium (the outer covering of the kidney) acetylsalicylic acid is contraindicated in nephritis (kidney inflammation). Other persons especially susceptible to undesirable effects of the drug are drunkards and persons with diabetes. In the latter groups, adverse effects show a special relation to the nervous system.—*J. Am. M. Ass.*

PNEUMONIA IN INFANCY AND CHILDHOOD*

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THE present communication is a report on pneumonia in infants and children. No attempt is made to review the voluminous literature on this subject. A comparison of various forms of treatment is made.

The histories of patients with clinically proved primary pneumonia are reviewed. No cases are included with complications, *e.g.*, prematurity, congenital heart disease, œsophageal atresia, nephritis, etc. Most of the patients were seen and examined clinically by one of us, and nasal or sputum cultures were examined by the method described by Auger.[1] Three methods of treatment were used as follows: (*a*) treatment, which mainly consisted of fluids by mouth, mustard applications to chest, aspirin by mouth, and in certain cases oxygen box or tent therapy; (*b*) sulfapyridine in adequate dosage, *i.e.*, blood levels of approximately 4 mg. per cent or over; (c) Type I pneumococcus rabbit serum in patients with Type I pneumococcus pneumonia.‡ In the 1937-38 group very few cultures of the sputum or nasal secretions were made, and in many instances blood cultures were not examined. In most patients in the 1938-39 group blood cultures were examined, sputum or nasal secretions were cultured, and x-ray examinations of the chest were made. The basis for a definite diagnosis was a positive history, positive physical findings, a typical clinical course, and positive x-ray and bacteriological findings in the cases in which these procedures were done.

The cases were divided for purposes of comparison into two groups, namely patients under 2 years of age and those from 2 to 14 years of age. In addition, pneumonia caused by all bacterial species and pneumococcus pneumonias were studied separately.

We have found that pneumonia under 2 years of age is usually of the broncho-pneumonic type as confirmed by post-mortem examination. During the year 1937-38, (October to September) 112 case histories were reviewed of patients who had uncomplicated pneumonia. During this year very few sputum cultures were examined. The duration of the disease in this group before treatment averaged 3 days. The course of the disease after treatment was inaugurated until clinical improvement (*i.e.*, marked fall in temperature curve and improvement or absence of chest findings) was found to be on an average 7 days. In other words, the average total duration of the disease in this group of 112 patients was 10 days. In this group there was a case fatality rate of 20 per cent. In the 1938-39 group (October to September) 28 patients were treated in the same manner adhered to before the use of specific therapy. The average duration of their illness before treatment was 3 days and 5.6 days after treatment. In this group the average total duration of the disease was 8.6 days. Sputum or nasal cultures were for the most part examined in this group, and include pneumonias caused by pneumococcus, streptococcus, staphylococcus, *B. influenzæ* and mixtures of these bacteria. In this small group of 28 we found a case fatality rate of 18 per cent, which is practically the same as in the 1937-38 group under 2 years of age. In the 1938-39 group, 53 patients were treated with sulfapyridine in adequate doses. The average duration of the disease before treatment was 3.4 days and after treatment 3.3 days, or an average total duration of their disease of 6.7 days, which is a shorter course than the two previous groups treated by the usual non-specific methods. In this group treated with sulfapyridine the case fatality rate was reduced to 5.6 per cent.

In Table II it is readily seen that there were only a few patients in the group treated by usual methods and by sulfapyridine. It is noteworthy to observe that the average total duration of the disease in the non-specific treated

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From the Wards and Laboratories of the Hospital for Sick Children, Toronto, and the Department of Pædiatrics and Connaught Laboratories, University of Toronto.

† Working under a grant from the Banting Research Foundation.

‡ Type I Pneumococcus Rabbit Serum was kindly supplied by the Connaught Laboratories, University of Toronto.

group was 7.6 days as compared to 6.2 days in the sulfapyridine treated group.

In this group of patients aged from 2 to 14, the years 1937-38 and 1938-39 are compared. In the 1937-38 group cultures for the most part were not made. In the 1937-38 group 179 non-specifically treated patients showed a total average duration of their disease of 3 days before treatment and 5.4 days after treatment, or an average total duration of 8.4 days. In 1938-39 pneumonia in patients from 2 to 14 years of age was caused by the pneumococcus of the various types in approximately 90 per cent of cases. There were so few patients with proved pneumonia caused by other bacteria that they have not been included in the 1938-39 group. In the 1938-39 group, 48 patients with pneumococcus pneumonia showed an average of 2.7 days before and 4.5 days after non-specific treatment, an average total duration of their disease of 7.2 days. In the 1938-39 group 70 patients with pneumococcus pneumonia of the various types were treated with sulfapyridine. The average number of days was 3 before and 2.6 after treatment, a total of 5.6 days. In the group of patients with pneumonia from 2 to 14 years of age in 1937-38 the case fatality rate was 1.6 per cent. There were no deaths in the 2 to 14 year group in 1938-39, either in patients treated by non-specific methods or in those in which sulfapyridine was used. In the 48 patients with pneumonia treated non-specifically in 1938-39, twenty-eight blood cultures were negative, and 20 were not done. In the 70 sulfapyridine-treated group, 62 blood cultures were negative, 1 positive, and 7 were not done.

In 1937-38, thirty-eight patients with Type I pneumococcus pneumonia showed an average duration of their disease of 3 days before non-specific treatment and 6.4 after treatment, a

TABLE I

PNEUMONIA, UNDER 2 YEARS

YEAR	PATIENTS	DURATION OF DISEASE DAYS 1 2 3 4 5 6 7 8 9	TREATMENT	SPUTUM CULTURE	C.F. RATE
1937-38	112	3 / 7	ROUTINE	NOT DONE	20%
1938-39	28	3 / 5.6	ROUTINE	ALL BACTERIA*	18%
1938-39	53	3.4 / 3.3	SP#	ALL BACTERIA	5.6%

* refers to pneumonias caused by pneumococcus, streptococcus, staphylococcus, B. influenzae, and mixed cultures.

SP = Sulphapyridine

▨ BEFORE TREATMENT

■ AFTER TREATMENT

TABLE II

PNEUMOCOCCUS PNEUMONIA, UNDER 2 YEARS, 1938-39

PATIENTS	DURATION DAYS 1 2 3 4 5 6 7	TREATMENT	DEATHS
18	2.6 / 5	ROUTINE	4
35	3 / 3.2	SP*	1

▨ BEFORE TREATMENT

■ AFTER TREATMENT

*SP = SULPHAPYRIDINE

TABLE III

PNEUMONIA, 2-14 YEARS

YEAR	PATIENTS	DURATION OF DISEASE DAYS 1 2 3 4 5 6 7 8 9	TREATMENT	SPUTUM CULTURE	C.F. RATE	BLOOD CULTURE
1937-38	179	3 / 5.4	ROUTINE	NOT DONE	1.6%*	NOT DONE
1938-39	48	2.7 / 4.5	ROUTINE	PNEUMOCOCCUS	0	28-20 ND[2]
1938-39	70	3 / 2.6	SP#	PNEUMOCOCCUS	0	62-1-7 ND[2]

*1.6% = 3 deaths in this group, 2 bronchopneumonia, 1 Type I septicaemia

= Sulphapyridine

[2]ND = Not done

▨ BEFORE TREATMENT

■ AFTER TREATMENT

TABLE IV

TYPE I PNEUMOCOCCUS PNEUMONIA AND EMPYEMA, 2-14 YEARS

YEAR	CASES	DURATION OF DISEASE DAYS 1 2 3 4 5 6 7 8 9	TYPE OF TREATMENT	EMPYEMA	B.C.	DEATHS	
1937-38	38	3 / 6.4	ROUTINE	11	8-30 ND[2]	2	
1938-39	22	3 / 6	ROUTINE	7	17-5 ND	1*	
1938-39	32	3 / 3	SP#	8	20-2 ND	0	
1938-39	19	3 / 2	SERUM	2	17-2 ND	0	

a = Blood cultures negative - Not done = ND

* = Death due to bronchopneumonia

= SP = Sulphapyridine therapy

▨ BEFORE TREATMENT

■ AFTER TREATMENT

total average duration of 9.4 days. In 1938-39, twenty-two patients with this type of pneumonia who were treated by non-specific methods showed an average of 3 days' duration of their disease before and 6 days' duration after treatment, an average total duration of 9 days. In the 1938-39 group, 32 patients with Type I pneumococcus pneumonia were treated with sulfapyridine in adequate doses. These patients showed an average duration of their disease of 3 days before and 3 days after treatment, or an average total duration of 6 days. In 1938-39, nineteen patients were treated with Type I pneumococcus rabbit serum by the continuous intravenous drip method. This group of patients had an average duration of their disease of 3 days prior to and 2 days after treatment, or an average total duration of 5 days. The numbers of patients developing empyema were as follows: non-specifically treated group, 1937-38, eleven out of 38 patients; non-specific treated group, 1938-39, seven out of 22 patients; sulfapyridine treated group, 1938-39, eight out of 32 patients; and the serum-treated group, 1938-39, two out of 19 patients. There were four immediate serum reactions in the serum treated group.

A review of the seasonal incidence of pneumonia in the two years reveals a slight rise in December of 1937 and a marked rise in the number of cases in June of 1938. In 1939, the main rise was in March with a smaller peak in May.

DISCUSSION

A few inferences are to be drawn from this report. In the first place, there is an appreciable difference between the case fatality rate in patients with pneumonia under 2 years of age and those with pneumonia between 2 to 14 years of age. In the group of patients under two years of age a reduction in the case fatality rate of 20 per cent in the non-specifically treated patients to 5.6 per cent in sulfapyridine treated patients is shown. In children between the ages of 2 to 14 years deaths from pneumococcus pneumonia are unusual with any form of treatment when the disease is primary and uncomplicated. On the other hand, there is ample evidence that the duration of the disease has been markedly reduced by specific therapy. It is seen that patients with pneumonia under 2 years of age in whom sulfapyridine was used respond more rapidly to this method of treatment than to older methods, and that the case fatality rate is reduced.

SUMMARY

Sulfapyridine has reduced the case fatality rate in patients under 2 years of age with pneumonia caused by various bacteria from 20 per cent in those treated non-specifically to 5.6 per cent in those receiving the drug.

Sulfapyridine has shortened the course of pneumococcus pneumonia in patients between 2 to 14 years of age. Deaths in this age-group are unusual with any form of treatment, providing the case is uncomplicated.

Sulfapyridine, used separately, and Type I anti-pneumococcus rabbit serum, used separately, have shortened the course of pneumonia in children between 2 to 14 years of age suffering from Type I pneumococcus pneumonia.

REFERENCE

1. AUGER, W. J.: *J. Pediat.*, 1939, **15**: 640.

RÉSUMÉ

Chez les enfants de 0 à 14 ans traités pour pneumonie, spécifique ou non, de 1937 à 1940 à l'hôpital des Enfants-Malades de Toronto, 3 méthodes ont été employées: (1) la méthode qui n'utilise ni sérum ni sulfapyridine; (2) la sulfapyridine seule, et (3) la sérothérapie antipneumococcique du type no. I. Seuls les cas non compliqués sont rapportés. Chez les enfants âgés de 0 à 2 ans le taux de mortalité est tombé de 20 à 6 pour cent grâce à la sulfapyridine. Chez ceux compris entre les âges de 2 et 14 ans la mort est rare quel que soit le traitement, mais la sulfapyridine a nettement écourté la durée de la maladie. La sérothérapie antipneumococcique du type no. I agit aussi bien que la sulfapyridine et abrège autant la maladie. Les séries récentes (1938-39) ont bénéficié des examens de contrôle et des recherches bactériologiques complètes. JEAN SAUCIER

According to statistics there has been a steady increase in the number of cases of mammary cancer for many years. For every eight women who in 1920 developed cancer of the breast, today there are eleven who do so, an increase of more than 35 per cent in twenty years. A part of this is due to the fact that there are a larger percentage of women today in the age-groups that are most likely to have cancer, some of the apparent increase may be credited to accurate diagnosis. Reports are based on more careful medical findings now than ever before. However, there is an unexplained actual increase and that emphasizes the importance of alertness for symptoms that may mean the disease is present.

THROMBOCYTOPENIC PURPURA*

BY LOUIS J. BRESLIN

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PETECHIAL hæmorrhage phenomena are, generally speaking, encountered in two groups of conditions: (1) thrombocytopenic states, either idiopathic or secondary, and (2) certain non-thrombocytopenic ones, such as purpura, aplastic anæmia, leukæmia, various septic and toxic states, and less often in pernicious anæmia, splenic anæmia, lipoid splenomegalies, benzol poisoning, etc. Such episodes may occur because of (1) allergy; (2) anoxæmic states; (3) toxins; (4) congenital weakness of the capillary wall; (5) vitamin C deficiency; (6) vitamin P deficiency; (7) disturbances in mechanism of blood coagulation, particularly with respect to the phase of thrombin formation. A reduction in the number of platelets is the outstanding feature, and the platelets may be large or small. Various investigators have ascribed the condition to disturbances of bone-marrow activity, replacement of megakaryocytes by other elements; others, to over rapid destruction of platelets in circulating blood, perhaps because of hypersplenism. Red blood cell formation is evidently not impaired, the major effect being due to stimulation of erythropoiesis because of hæmorrhage. Resistance of the red cells to isotonic solutions, although as a rule normal, is ofttimes increased, but may on the other hand be lessened. One usually for similar reasons encounters some degree of leucocytosis, although leucopenia may be present. The bone marrow is as a rule normal. Here, too, either increase or diminution of megakaryocytes may be seen.

This blood dyscrasia occurs at any age and in either sex. It is said, however, to be predominant among younger people, especially females. The mode of onset varies from acutely fulminant to extremely chronic. Usually there are spontaneous cycles of bleeding, clearing up only to recur after weeks to years. It is therefore impossible to prognosticate when purpuric manifestations are likely to disappear, and whether or not they will ever recur.

In addition to the low platelet count we can usually demonstrate prolongation of bleeding time, delayed or absent clot retraction, a positive tourniquet test, prothrombin and clotting time are as a rule normal, but may occasionally be prolonged and exhibit so-called re-clotting phenomenon. Post-mortem there is nothing diagnostic to be seen except hæmorrhages into various organs of the body, rarely affecting the lungs. The following chart will I believe prove to be of assistance when considering a differential diagnosis of the commoner hæmorrhagic blood dyscrasias.

Various therapeutic measures to combat this condition have been advised. Apparent benefit, noticed at times, can in part at least be ascribed to the tendency of the disease to undergo spontaneous remissions. Multiple transfusion, to overcome the immediate ill effects of hæmorrhage and to much lesser extent to replace platelets is indicated. Splenectomy at a properly selected time is unquestionably the treatment of choice. This as a rule is followed by increase in platelets and cessation of hæmorrhage, the latter even when platelet count does not return to anywhere near normal levels. Snake venom in the hands of Rosenthal and his group would appear at times to be of some value. The following is a brief history protocol illustrative of the difficulties encountered in attempting to make a diagnosis.

CASE REPORT

A.H., a white married male, aged 25 years, born in Ireland. For the past 8 years he had suffered from profuse spontaneous epistaxis, spontaneous eruptions of petechiæ all over the body. He volunteered the information that he would ooze blood for 15 to 30 minutes from the slightest cut or abrasions. Two years ago he underwent a nasal operation and almost bled to death. His family and past medical histories were otherwise unimportant. He was admitted to the medical service of the Mount Sinai Hospital on January 16, 1940, because of recurrence of this complaint; discharged in July, 1940.

Physical examination was essentially negative, revealing a very pale thin young male, lying comfortably in bed. The head, face, and neck region were normal except for a deformity of the nose (old fracture). Some fresh blood was seen in the naso-pharynx; nose, mouth and gums were pale, firm, but bleeding readily. Scattered all over the body were small discrete petechiæ, varying in size from a pin head to split pea. These were raised and could not be obliterated by pressure. Heart and lungs normal; blood pressure 100/60; pulse rate 70 to 80; temperature, normal. No adenopathy or splenomegaly, etc., was noted. The edge

* From the Medical Division of the Mount Sinai Hospital, Toronto.

of the liver was just palpable. Red blood count, 1,450,000; hgb. (Sahli corrected) 36 per cent; colour-index 1.3; 1.5 per cent of reticulocytes were present; some anisocytosis, poikylocytosis, very occasional monocytes; lymphocytes 62 per cent; no immature cells seen. Bleeding-time varied from 6 to 16 minutes; clotting time 2 to 3 minutes. The tourniquet test was decidedly positive. Clot retraction was poor, van den Bergh 0.3 to 0.4. Urine, specific gravity 1.019; free of albumin, sugar, red or white blood cells, casts; no urobilin present. The gastric contents showed the presence of free HCl. No melæna. Multiple transfusions were given by the indirect method; a high caloric anti-anæmic diet with ample vitamins was instituted, likewise ferrous salts, liver, etc. Despite an occasional rise of the red blood cells to 3,560,000, with hgb. to 55 per cent he continued to be much the same as upon the date of admission.

Two sternal punctures were done and disclosed a moderately active normal marrow, *viz.*, normoblasts and a few erythroblasts, myelocytes and promyelocytes, mature red and white blood cells. Megakaryocytes appeared to be diminished in number but of mature form. Because of repeated recurrences of petechiæ and spontaneous hæmorrhages from the nose, and despite far from convincing evidence that this was a case of idiopathic thrombocytopenia purpura splenectomy was uneventfully performed on April 8, 1940. Histology of the organ thus removed revealed nothing pathognomonic of any specific condition. There was congestion of the spleen and hyperplasia of its follicles.

His course to date has been as follows. He feels stronger, and has with one exception been free from epistaxis and petechiæ. He recently underwent circumcision because of troublesome phimosis, without exhibiting any undue bleeding. Blood count and hæmoglobin stay at about 2.5 millions and 51 per cent; platelets 200,000 or over. Repeated examination of blood smears however fail to exhibit a reticulocyte response above 1.5 per cent; an occasional normoblast seen; white blood count, with two exceptions, has been 4,500 to 5,000. No premature cells noted; relative lymphocytosis present.

	Hæmophilia	*Thombocytic purpura*	*Aplastic anæmia*	*Aleukæmic leukæmia*	*Agranulocytosis*
Age	young	young	?	childhood	young
Sex	males (females transmit)	both sexes	both sexes	both sexes	both sexes
Anæmia	± to ++ after hæmorrhage	± to ++ after hæmorrhage	+++	+++	slight
Red blood cell activity	normal	normal to ++ (hæmorrhage)	poor or none	good	normal
Platelet count ...	normal	markedly decreased	decreased	decreased	normal
White blood cell activity	normal	+ or normal, occasional –	progressive decrease, relative lymphocytosis	premature cells	no polymorphonuclears, relative lymphocytosis
Bone marrow remission	normal	normal – + after hæmorrhage	poor except with remission	active	few polymorphonuclears; may imitate leukæmia in remission
Bleeding time ...	normal, occasional +	+++	+	normal or +	normal
Coagulation time	+++	normal (occasional slight +)	at times prolonged	at times prolonged	normal
Clot retraction ..	normal	absent or delayed	normal to slight + or –	normal to slight + or –	normal
Tourniquet	absent	present	±	±	±
Prothrombin time	prolonged	normal	normal to slight +	normal to slight +	normal
Petechial	rare	+++ spontaneous	++	++	+
Joint hæmorrhages	common, especially with trauma	rare	rare	±	absent
Splenomegaly ...	?	39% + 19% –	?	+	+
Adenopathy	none	none	none	tender	rarely
Angina	absent	absent	+	++	+
Fever	?	+ in acute cases	+	+++	+
Increase of van den Bergh.	±	± to –	+	+	±

DISCUSSION

The long duration of this condition, commencing in early youth, freedom so far as can be ascertained from exposure to benzol, radium, x-rays or other myelotoxic substances, periodic spontaneous recurrence of petechiæ and hæmorrhages, a persistently low platelet count in the absence of splenomegaly, accompanied by prolonged bleeding time, very poor clot retraction, positive tourniquet tests, normal clotting time, absence of premature cells in the peripheral blood, normal bone marrow, and now a tendency toward higher, and even normal platelet counts are findings in favour of the diagnosis of thrombocytopenic purpura. Low white blood counts are occasionally encountered in this condition.

The low level of regeneration of the other myeloid elements, *viz.*, low white blood cell, relative lymphocytosis, low red blood cell, reticulocyte counts and hæmoglobin count, make one strongly suspicious of an aplastic anæmia. The values thus obtained, although not consistent with the amount of bleeding, are stationary rather than progressively decreasing. Three bone-marrow examinations have to date failed to substantiate or actually disprove this diagnosis.

The patient's improvement so far and almost total freedom from recurrences of petechiæ, etc., may merely be part of a spontaneous remission so common in this condition. Splenectomy has, apparently at least, done no harm. One will have to make further bone marrow and peripheral blood studies before reaching a positive diagnosis.

SCHOOL HEALTH PROBLEMS*

By Lloyd P. MacHaffie

School Medical Officer, Ottawa Public Schools, Ottawa

A MORE comprehensive heading for what I have to say today would be "School Health Problems and their Relationship to Pædiatricians and Family Physicians"; for in my opinion no school health service can function efficiently without the sympathetic co-operation of the medical fraternity.

I have been school medical officer for the Ottawa Public Schools for almost ten years. I have talked to various medical officers in Canada, the United States, and Great Britain and have studied numerous annual reports of school health services. It seems to me that all are faced with similar problems and difficulties. In case any of my audience are unconvinced that there should be health programs in the schools I might indicate some of the valuable services which they offer and which are not offered in any other way to the school-age child.

1. *Physical examinations.*—(*a*) Of the children coming from poorer homes: those on relief and the low-wage earners. If periodical physical examinations and inspections are advisable for all school children there must be school medical inspection. There are facilities for the examination and treatment of the poor sick child but not for the poor child with defects. (*b*) Of the children whose parents have the means to pay for medical attention. Many of these children receive annual or more frequent examinations, but defects may develop between visits to the doctor. Then, too, there are certain defects which are seldom looked for on these visits. Many children, even from the well-to-do class, are not taken to the doctor unless they appear ill or below par. The insidious development of some illness or a potential illness-producing defect may be detected at the school examination, which when reported to the family doctor may result in the rapid correction of the underlying condition before severe damage is done, with little or no loss of school attendance and a financial saving.

2. *Environmental supervision and inspection.*—Lighting, sanitation, ventilation and heating need constant medical supervision. School boards must be impressed with the desirability and urgency of correcting defective conditions. School lighting is deplorably inadequate in most schools and may to a large extent account for the great prevalence of visual defects and eye-strain.

3. *Health education.*—The present trend is to leave more and more of the responsibility for this to the teaching staff. But the school medical officer and the nurses should act in an advisory capacity. They cannot escape the responsibility altogether; their opportunities of teaching health matters are too apparent. Parental education through home and school clubs, church organizations, service clubs, and the press should be adequately dealt with by the school medical officer. Health pamphlets and bulletins on current and pertinent health subjects should be distributed to the parents and teachers.

4. *Preventive medicine.*—(*a*) Vaccination and the giving of toxoid appear to be developing more and more into school projects in spite of

* Read at the Seventy-first Annual Meeting of the Canadian Medical Association, Section of Pædiatrics, Toronto, June 21, 1940.

the desire of health and school authorities to place this responsibility on the family doctor and pædiatrician. Only where compulsory pre-school vaccination is enforced are school authorities relieved. Recently, in the City of Ottawa, the local health authorities held vaccination clinics in all elementary schools—public and separate; in our public schools 4,500 pupils were vaccinated. In spite of radio talks on vaccination, distribution of literature, and the presence of free facilities in the city health centres, only 12 to 15 per cent of our school population was vaccinated. School clinics turned out to be the solution. It is more than likely that when our figures have been finally analyzed they will show that 75 to 80 per cent of our pupils have been immunized to smallpox. The response to consent cards was surprisingly excellent, the way having been paved by a short but comprehensive press and radio campaign.

A very deplorable situation in respect to the incidence of diphtheria was present in Ottawa a few years ago. In spite of a fair amount of toxoiding by the family doctors, pædiatricians, and health clinics no headway was made until the institution of annual school toxoid clinics by the health department. I believe that problem has to be handled in a similar fashion in most communities.

(*b*) Inspections of pupils in classrooms and of pupils readmitted after illness, and the detection and exclusion of minor and major communicable disease and suspect scarlet-fever carriers constitute important features of the school health program. Without the closest surveillance by the school health services our schools would be great sources of contagion, in spite of the alertness of teachers.

5. *Dental clinics.*—The care of the teeth is one of the greatest problems with which Boards of Education are saddled. A great many of the children of those with means do not visit their dentist twice yearly, and preventive dentistry does not exist for the poorer children. The responsibility of detecting dental defects is usually that of the school nurses and the school medical officer, although school dental officers frequently make dental surveys. School Boards have had to establish dental clinics for poorer school children because no other authority will do so.

6. *Nutrition.* — The frequent weighing and measuring of school children, taken along with other factors, offers an extremely valuable check on the state of the nutrition and health of the child. This service cannot be obtained elsewhere. If the findings are properly interpreted along with proper follow-up—health talks to children and contacts with parents—considerable benefit will accrue to the children.

WHAT A SCHOOL HEALTH SERVICE DOES NOT DO

It does not attempt medical treatment other than the giving of first-aid treatment to minor cuts, abrasions, burns and bruises, etc. Sometimes school health services have found it necessary, however, much to their dislike, to treat scabies and pediculosis. Parents are notified by letter or by personal contact of any encountered defect and advised to consult their physicians. The school examination, although frequently called complete, is nevertheless far from such. Tuberculin, blood and urine tests are only rarely performed. The child's physician or hospital clinic must complete the examination.

HOW MAY THE CHILD'S PHYSICIAN CO-OPERATE?

(*a*) Assume a greater degree of responsibility in respect to all recognized proved methods of immunization — definitely pre-school procedures.

(*b*) When periodical examinations are made by the family physician or pædiatrician might I humbly suggest that vision and hearing tests constitute part of the examination? These will yield a rich harvest. Might I also suggest that a greater interest be taken in static foot conditions? They are very prevalent.

(*c*) I should like to see iodine administration for the prevention of juvenile goitre as much a part of the physician's stock-in-trade as cod liver oil and orange juice.

(*d*) Might I also suggest that sick children be not given weak tea to drink? Teachers, school medical officers and nurses spend hours every week teaching children the value of drinking milk. Coffee and tea drinking, to the exclusion of milk, is one of our greatest problems, and, along with late hours of retiring, is a prime cause of failure to gain in weight.

(*e*) Physicians could be of great assistance if they refused to issue medical certificates for children to return to school after absence with communicable disease unless they have seen the

child, and also if they refused to issue certificates on the basis of statements made by the parents. I regret to state that this is a not uncommon or localized practice. German measles may sometimes be scarlet-fever; hives, very frequently chicken-pox; and glands in the neck, mumps, etc.

Schools with modern up-to-date school health services and alert teachers give a tremendous amount of time and labour to contagious disease control. Parental co-operation is poor, but very critical; medical co-operation is far from ideal. A public health-conscious medical fraternity would be desirable.

The Pre-school Child

I should like to make a few remarks about the child of this age-group. The opinion of school medical officers the world over is that many of the pronounced defects which handicap children in their school work had their onset prior to the children's entry into school. Meticulous care is offered in most communities to all infants and to school children, but there is an alarming hiatus as affecting the pre-school child—a gap which remains open until the school period arrives when medical inspection gathers the "forgotten child" under its wing and endeavours to cope with its health problems. All through the school period special classes have to be devised for many of these children with heart, hearing, visual and crippling defects; many non-remedial defects have developed, such as permanent deafness from the neglected suppurating ear and earache, or loss of sight in one eye from parental complacency in regard to squint.

What is the Solution?

Firstly, increased free clinical facilities for continuous medical supervision from birth to the school period. Secondly, parental education by alert and well informed medical opinion, aimed to overcome that dangerous triad of apathy, indifference, and ignorance shown by so many parents. Parents must be made to realize that while Johnny is outgrowing rheumatism he may be developing heart disease; while outgrowing squint he may be growing blind; and while outgrowing earache or "bealing" ears he may be growing deaf—and so on *ad infinitum* with the pathetic story.

This attitude of *laissez faire* is responsible for much preventable ill health, future suffering and expense, for the health of to-day's child determines in a large measure the health of tomorrow's adult and the citizen of the future.

Résumé

Les écoles devraient avoir des programmes de santé. L'examen physique périodique peut corriger et guérir des petites défectuosités avant qu'elles deviennent permanentes ou incurables. L'école et le milieu familial doivent étudiés et améliorés s'il y a lieu. On doit enseigner les principes sanitaires. Les enfants sont déjà vaccinés contre quelques maladies, mais on doit les éclairer ainsi que leurs parents sur toutes les maladies évitables. Le dentiste devrait voir tous les écoliers deux fois par année. Il est facile de les peser et de mesurer leur taille régulièrement. Il est aussi facile de généraliser à l'examen du sang et des urines et de faire l'épreuve à la tuberculine. La collaboration entière du milieu familial est indispensable aussi bien pour l'écolier que pour l'enfant qui ne va pas encore à l'école. Pour faciliter la solution du problême il faut multiplier les examens préscolaires, éduquer les parents et lutter contre la tendance au moindre effort.

Jean Saucier

Skim-milk, perhaps because of a popular old advertisement, is a rather opprobrious term, and the prejudice against this product in America is such that according to the U.S. Department of Agriculture only about 12 per cent of the skim-milk produced is used in the manufacture of dairy products. In a paper by Mr. J. S. Abbott at the sixty-ninth annual meeting of the American Public Health Association it was urged that the misuse of skim-milk constitutes an enormous economic waste. It contains all the essentials of whole milk except the milk fat and fat-soluble vitamins, and it even contains a certain amount of each of these, though not so much as whole milk. The Nutrition Committee of the League of Nations stated that, pint for pint, skim-milk contains more calcium, phosphorus, iron, and protein (though, of course, fewer calories) than whole milk, and is much cheaper. It is a good foodstuff for animals, but to feed it to pigs is unsound economics because it requires 10 pounds of the food nutrients in skim-milk to produce 1 pound of food nutrients in the form of pork. Industry and legislative effort to create a market for this wholesome foodstuff, says the author of the American paper, would be in the interest of consumers and dairy farmers alike, and there ought not to be any restrictions or discriminations against compounding skim-milk with other foodstuffs for use as human food in the manufacture of food products that supply a want of the people and that can be produced economically to advantage.—*Brit. M. J.*, 1941, **1**: 51.

THE OVERWEIGHT CHILD*

BY LIONEL M. LINDSAY

Montreal

IN a pædiatric practice many children are encountered whose chief complaint is that of being considerably overweight. Often this condition of the child is accepted by the parents as a sign of good health and digestion, and indeed the child may appear so robust and cheerful that any criticism of his weight is resented.

On the other hand, some children are brought to their physician because obesity is the cause of a definite handicap, mental or physical. They may be taunted by their companions until they become acutely sensitive of their appearance, or they are unable to participate in games, and so become less active and still heavier. The overweight girl may realize that she is not as attractive as her more slender companions. These effects may in time lead to definite personality changes or behaviour problems which may be detrimental to the whole future of the individual. Fortunately, such an eventuality is not the rule, for many obese children will assume a more normal configuration as adolescence advances, and many are cheerful in spite of their weight.

For practical purposes, any child may be considered overweight who is more than 20 per cent above the average weight for age, height and sex when compared with standard tables. All grades may be seen, even to those who are double their expected weight. Some observers claim that obesity may be gauged more accurately by clinical inspection than by height and weight tables, for then the distribution of fat and general physique may be taken into consideration.

It is generally assumed that the increase in weight of this type of child is due largely to an increase of adipose tissue. This is not always the case. Overweight children are frequently above the average in height. Their bones appear to be larger, and it has been shown that their weight is due as much to increase in muscle as to fat. Sexual development occurs somewhat earlier than in the average child. In short, the overweight child is often bigger and stronger than his slimmer companion. But the greater strength is sometimes counteracted by the greater load he has to carry, and so he may become somewhat cumbersome or complain of a variety of symptoms, such as dyspnœa, flat feet, or pains in the back or legs. Such symptoms would make the child less active, and so a vicious circle is established. He becomes indolent and lazy, and so heavier. But generally speaking stout children are particularly cheerful and bright and their round, rosy faces are a pleasure to behold.

The onset of obesity may be quite rapid, beginning usually when the child is between 8 and 12 years of age. Sometimes the onset dates from an illness or operation, at other times it develops more insidiously. The cause may be difficult to ascertain, and the pathogenesis is uncertain. Heredity is a very definite factor. Often one or both parents is decidedly large or obese and the offspring may be strikingly large, even in early childhood. Such children may have an abnormally large appetite, especially for carbohydrates, but this in itself does not necessarily lead to obesity. Many a "skinny" child will consume a comparable amount of food without noticeably increasing his weight.

When the obesity appears to be caused by overeating or lack of exercise it is said to be of exogenous origin. When it occurs as a constitutional abnormality, (probably hormonal) it is designated as endogenous. Authorities on the subject differ widely in their opinions regarding the relative importance of these two causes.

It would seem that while some overweight children fall definitely into the exogenous category, and some are obviously the victims of endocrine disturbance, the majority may be grouped between these two extremes. All are the result of a peculiar metabolism, which in the last analysis is probably governed by glandular action. This would seem to account for the tendency of boys and girls to put on excess weight at the time of puberty, and later,

* Read at the Seventy-first Annual Meeting of the Canadian Medical Association, Section of Pædiatrics, Toronto, June 19, 1940.

as the glands become harmonized, the adolescent assumes more normal proportions.

It has humorously been suggested that the obese child may be classified as, the enviable, the comical, and the pitiable. Obviously those in the first class would require no treatment. The others require some consideration. The fat boy in "Pickwick" might be considered both comical and pitiable.

It is necessary then before undertaking treatment to consider the individual case in all its aspects. The heredity and physique of the child's forebears indicate the child's possible tendencies. The eating habits of the child must be ascertained, especially in regard to the nature of the foods which he likes and dislikes and his habit of eating between meals. An estimate of the amount of exercise he takes is also necessary. The age of onset of his obesity and the manner of its development may suggest a clue to its underlying cause.

The physical examination will reveal the child's general physique, the distribution of fat, the texture of his skin and hair, and the sexual development. If the condition seems to warrant further investigation one may require a basal metabolic rate, x-ray films of the sella turcica and centres of ossification. A determination of the sugar tolerance, specific dynamic action, and the creatinine coefficient may also be required. Yet it is surprising how seldom one finds any abnormality by these tests.

However, by such means a certain number of cases will be found which can be classed as due to endocrine dysfunction. One must bear in mind that the basal metabolism rate of the overweight child cannot be measured by the same standards as the average child. The most accurate readings are perhaps obtained when computed on the basis of height rather than on the usual surface area.

Hypofunction of the thyroid or the pituitary gland are by far the commonest disturbances which lead to obesity of more or less characteristic type. The term Fröhlich's syndrome, or dystrophia adiposo-genitalis, is rather loosely used to designate an overweight child with particularly small genitals. True instances of this are not common. The syndrome is probably caused by some lesion in the hypothalamus associated with impaired function of the hypophysis. Occasionally one encounters obesity resulting from tumours or hypertrophy of the adrenal cortex or of the gonads. Other glandular disturbances may be associated with these and the pattern becomes intricate.

Before advocating treatment still other things must be taken into consideration. In the first place, if the child is strong and healthy, and is not concerned with his or her appearance, and not suffering from any complaint that might be attributed to his weight, it would seem advisable to be conservative and to keep the case under observation. Natural growth and development may bring about an amelioration of his condition with the minimum of interference. But if normal activity is hampered, and the child complains of dyspnœa, pains in his legs and feet, and, particularly, if he is sensitive about his appearance, some effort should be made to improve the condition. The importance of the psychological factors in this regard have been stressed by Dr. Bruch, of New York. The child often resorts to eating as a solace to his wounded pride or handicap in not being able to compete with his fellows.

The first essential in the treatment is to secure the co-operation of both parent and child. Without this one can hope to accomplish little. Eating is a pleasant pastime which may become pathological. The indulgent mother may develop in her child the habit of stuffing himself with ice cream and cake at all times of the day. To break this habit will be a real struggle. The child should be protected from the temptations of the pantry. Tact will be necessary and the child may be allowed an apple or pear between means in order to appease his appetite. It is understood that lapses from grace are apt to occur and must be condoned.

Whether the obesity is considered as due to exogenous causes or endocrine disturbance, reduction in the amount of food consumed will produce a loss of weight. Discretion must be exercised in restricting the diet of children, especially at the period of rapid growth and development, when normally large quantities of food are consumed. It would be unwise and perhaps detrimental to advise any drastic cut in calories at this time. But the total calories may be considerably reduced by limiting the consumption of fats and carbohydrates, provided a liberal amount of protein and green vegetables is allowed. These not only satisfy the appetite but also supply the physiological needs of the patient. Moreover a high protein diet tends to stimulate metabolism and thus prevents the

storage of fat. There is a tendency in obesity for the tissues to hold an abnormal amount of water, and so it would seem rational to restrict the quantity of water and salt consumed by the patient.

General rules for the regulation of the diet are usually sufficient, at least in beginning treatment. The following have been found satisfactory.

Do not eat: fried food, sausages, pork, salt fish, cake, candy, jam, syrup, ice cream, pastry.

Eat small quantities of bread, potato and butter. Eat largely of green vegetables, salads and fresh fruits, lean meat, cheese and fish. Take 30 ounces of milk daily, but no cream. Buttermilk or skimmed milk is sometimes preferable. Take only one small glass, (six ounces) of water before or during the meal. No table salt should be added at meals. Additional fat-soluble vitamins should be given.

If these instructions are carefully followed and do not bring about an improvement a more specific diet providing for 1,500 or 2,000 calories may be prescribed. By such means a stationary or even reduced weight will produce the desired results, for the child will continue to grow in height and so assume more graceful proportions. The importance of an adequate amount of protein, calcium and vitamin D at puberty must be stressed. The development of slipped epiphysis and epiphysiolysis at this age has been attributed at least in part to an insufficiency of these elements in the diet.

Secondly. Increased activity should be encouraged, beginning with gentle exercises and increasing in proportion to the child's tolerance. Swimming and bicycling are perhaps two of the most suitable forms of exercise for those children whose weight definitely hampers their movements.

Some of these patients may be indolent and lazy, and may require a certain amount of urging to keep at their exercises. They may be discouraged by their lack of skill and success in games and by the derision of their playmates. To these small doses of benzedrine sulphate may be given with benefit. This drug not only stimulates physical activity but is said to have a definite effect in depressing the appetite. Small doses may be given once or twice daily, preferably in the forenoon.

Perhaps the most widely used remedy for reducing weight is thyroid extract, irrespective of whether there are signs of hypothyroidism or not. Thyroid does increase the rate of cell oxidation and so burns up fat. It also tends to withdraw water from the system. Usually it has very little effect in raising the basal metabolic rate in cases which are not frankly myxœdematous. Nevertheless, small doses under controlled conditions can be given, certainly without harm, and often with benefit, especially at puberty.

Pituitary preparations have their advocates, but the accredited results are not always convincing. Given by mouth, they have little effect, while the trouble and expense of giving them hypodermically is only justified under very exceptional circumstances.

In conclusion it must be admitted that the treatment for the overweight child, as outlined above, does not change the constitution of the patient nor correct a disturbance in the endocrine system and so can only be said to be palliative. Nevertheless, if carried out consistently, it will alleviate the condition to some extent until such time as nature can establish a more normal balance of the fat regulating mechanism. It will also tend to prevent the development of psychological problems and of mechanical disabilities during the vulnerable period of adolescence.

POWDER ON GLOVES RESPONSIBLE FOR ILLNESS.—Serious complications and illness may follow operations if talcum powder from the surgeon's gloves gets into the surgical wound. Drs. Edward J. McCormick and Thomas L. Ramsey report two cases of post-operative complications in which second operations were required, one of them resulting in the loss of the child-bearing organs in a 21-year-old woman. In both cases crystals of magnesium silicate, or talc, were found in the inflamed tissues removed at the second operations. It is probable that many other cases of post-operative complications caused by talcum or by lycopodium powder have gone undiagnosed in the past. Careful washing of the gloved hands of the surgeon and his assistants, to remove the powder used on the gloves, and care to keep the air of the operating room free of the powder are urged to prevent such complications.—*Science News Letter*, March 15, 1941.

Case Reports

A CASE OF RUBEOLA DURING THE PUERPERIUM

By M. Lerner

Cut Knife, Sask.

I am reporting this case of measles during the puerperium because of its rarity and the successful treatment of this serious association.

Mrs. W.R., aged 20, para-i, grav-ii, was admitted to the Cut Knife Municipal Hospital on October 20, 1940, at about 4.30 p.m. She was having labour pains at 5 minute intervals, and complained of having a "cold", and a dry hacking cough. There being a measles epidemic in the district, she was questioned, and admitted that she was a contact and that she had not had the disease previously.

The labour was normal and she was delivered of a male child weighing 8 pounds. The patient and baby were isolated.

The following morning, October 21st, on examination, Koplik spots were seen on the buccal mucous membrane. The patient was given 20 c.c. of her husband's blood intramuscularly, the latter having had measles some ten years before. The baby also received 20 c.c. of blood from the same donor into the gluteal region. The baby was taken off the breast and separately isolated. That day the patient's cough became worse and her temperature rose to 102° at 4 p.m.

On October 22nd a rash appeared, typical in type and distribution. The patient was miserable, and the temperature climbed to 103.° She was given, in addition to the usual prescribed treatment, prontylin, gr. 10, $NaHCO_3$ gr. 10, and methylene blue, gr. 1, O.H.8.

On October 23rd the rash had appeared all over her body, and while abundant on the upper half the spots were scarce on her lower limbs. Her eyes were extremely painful, but her temperature had dropped to normal.

The following day her temperature rose to but 99.4°, dropped to normal on the next, and remained there until the day of her discharge, October 31, 1940. The rash began to fade on October 24th and was completely gone by the 26th.

The baby showed no signs of illness or rash and 3 weeks after birth there is no evidence of measles.

I believe that the blood injection, though given late, modified the course of the disease in the case of the mother and prevented it in the baby. The prontylin no doubt prevented secondary infection from setting in.

TREATMENT FOR DERMATITIS VENENATA

By K. A. Baird

West Saint John, N.B.

Even four swallows "do not make a summer", nor do four cases prove the value of a treatment, but the following case histories seem to suggest a useful line of treatment for poison ivy dermatitis, especially in view of the paucity of the information given in any books the writer has been able to consult.

R.H., female, aged 20.

Complaint.—Blistering on the right buttock said to have been caused by poison ivy. She had been getting a typical allergic reaction to something in various parts of the body for the last two weeks since contact occurred. Now she had a rash on one thigh which gave a burning sensation. The patient was given 10 c.c. of 10 per cent calcium glucono-galacto-gluconate* intravenously. The rash on the thigh faded in a few minutes and the discomfort was relieved. She was given prescriptions for ephedrine hydrochloride (gr. ½) and calcium gluconate, to take orally if symptoms returned. She reported later that the condition did not return.

G.H., a male, aged about 21.

This young man was working around poison ivy four days before and got a severe dermatitis on face, arms, hands, legs, etc. He continued to react severely and the rash "burned" very much at times. He was given 10 c.c. of 10 per cent calcium glucono-galacto-gluconate intravenously. The patient fainted briefly from psychosis as he had never "had the needle" before. He recovered promptly from the faint and said he was relieved of the burning sensation. The rash paled somewhat. He was given prescriptions for calcium gluconate, ephedrine hydrochloride tablets, and a soothing ointment. He promised to return if not definitely better, but he did not return.

R.W., a male, aged about 58.

Complaint.—Pain and swelling of both eyelids and tissues, and blebs over the left side of the forehead.

History.—The fact that this man had psoriasis on his arms and abdomen for the last ten years does not seem to have any bearing on the present case. Eight days ago his forehead broke out in a pimply rash. The area was very tender. It started at the outer margin of the left eye and extended up over his forehead. Three days later his left eye was closed and the swelling had spread to the right eye and down the left side of the face. The affected area was very sore and throbbing. Eight days after the initial lesion, the appearance was that of an allergic reaction rather than herpes, and was still smarting and stinging, but he said he felt somewhat better. The patient attributed his trouble to flies (which were thick) or to some plants with which he came in contact while working around with weeds. He was admitted to hospital. His temperature was 101° on the evening of the day of admission, but otherwise remained within normal limits. He was given calcium intravenously on three consecutive days as well as calcium lactate (gr. 10 t.i.d.). The condition rapidly improved, the swelling subsided, and the rash dried and disappeared in three or four days.

G.A., a druggist, came to the office with an acute dermatitis on both hands and forehead. His arms and hands were noticeably swollen, and he said that they felt tight when his fingers were flexed. He attributed the condition to exposure to poison ivy four days before. He had been treating the area himself by frequent applications of Dakin's solution and tincture of iron. He was given 10 c.c. of calcium glucono-galacto-gluconate intravenously. Within a few minutes he reported that his hands felt less swollen. He was advised to take calcium gluconate by mouth, and he was to take ½ gr. of ephedrine if any severe symptoms developed. The condition continued to improve rapidly, the red rash fading and the swelling being reduced. Within two or three days the patient considered himself cured.

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* Calcium glucono-galacto-gluconate "Calcium Sandoz" is the new formula prepared by Sandoz Laboratories.

Editorial

PEPTIC ULCER—THE MAJOR DISABILITY OF WARTIME

AN epigram attributed to the Emperor the First runs thus: "An army marches on its stomach." This pronouncement is as true today as it was then, though it has now a connotation different from that in the mind of the great conqueror. Then it had reference to the importance of maintaining communications; now it concerns the gastro-intestinal tract of the personnel. Of late it has become increasingly evident that disorders of the alimentary tract—peptic ulcer in particular—must be regarded as the major medical disability of wartime.

So frequent were the ulcer cases during the early months of the war that a Commission was appointed in Britain under the auspices of the the Leverhulme Fund of the Royal College of Physicians to investigate the subject. During the period that elapsed between the dispatch of the first troops of the British Expeditionary Force to France and April 29th, 1940, of all the cases evacuated to the United Kingdom 12.5 per cent carried a primary diagnosis of gastric or duodenal disease. If the emergency evacuations of the base hospitals were excluded, since even those with minor illnesses were sent home, the figure rose to 14.4 per cent.[1]

This matter concerns us here in Canada, for many of our men are now returning, invalided out of the service, and we are informed on excellent authority that the proportion of peptic ulcer cases among them is surprisingly high.

According to the study of the situation by the Commission above referred to the cases of digestive upset could be placed in four categories—malingering, neuroses, gastritis, and peptic ulcer. The correct diagnosis is highly important, but, obviously, not easy. It has been advised by Sir Arthur Hurst that special hospitals be set up, staffed by specialists in gastroenterology, who would make the diagnoses on scientific principles. We have not reached that point yet in Canada, however.

It is not pertinent to our purpose to discuss the pathological problems involved in the production of peptic ulcer, but we will refer to certain of the etiological factors which, though of a secondary nature in the evolution of the condition, are of prime importance in our present problem. They are: family idiosyncrasy, unsuitable food, overwork, and worry. If these factors are operative under peace conditions, as we believe they are, their action will, we would expect, be intensified under the exigencies of war service.

In the opinion of the Commission the most important single factor in the causation of peptic ulcer is the change from the selected diet of home to the rigid routine of the army ration. They noted, too, that 38 per cent of the ulcer patients had teeth inadequate for their task, though only 15 per cent gave evidence of dental sepsis. Further, it is important to note that in nearly every case the man had had his ulcer *before* the war. When at home under ordinary conditions the would-be recruit has been able to select his diet to suit his needs; in the army he cannot do so. At home he can rest when he feels like it; in the army he may be exercised beyond his limit of endurance. At home his worries can sometimes be avoided or lessened; in the army they are unavoidable and more intense.

Elsewhere in this issue (p. 525) can be found a Table furnished by Major-General LaFlèche, of the National War Services Department, which gives us illuminating statistics as to the prevalence of the various disabilities found on the examination of applicants for admission to military service. The figures are based on the records of 10,000 men. As might be expected the chief disability was defective vision, necessitating the use of glasses—14.14 per cent; stomach and intestinal disorders, among which, no doubt, peptic ulcer is included, second highest on the list—8.44; foot troubles —8.36. This second figure will help to support the thesis that peptic ulcer is common in peace time as well as in war time. It is gratifying to note, however, that tuberculosis is not common among the

1. PAYNE, R. T. AND NEWMAN, C.: Interim report on dyspepsia in the army, *Brit. M. J.*, 1940, **2**: 819.

applicants—0.74 per cent. We are not told what percentage had defective teeth, but 3.52 wore dentures.

The moral of all this, is, of course, that every effort should be made to avoid enlisting men with peptic ulcers. Under the conditions of the preliminary routine examination it is easy to miss these cases. We may have to deal with the man who minimizes his symptoms in his eagerness to be accepted; and we, on the other hand, may meet the man who in his desire to escape enlistment gives a fake history or exaggerates the symptoms he has. Generally-speaking, if the candidate has had severe symptoms he will have been referred by his doctor to some hospital for x-ray examination, and it should be possible to get a report on his condition. And once an ulcer, always an ulcer!

This matter of peptic ulcer is of sufficient importance to call for a definite course of action and concerted action. The time for the detection of peptic ulcer is before the candidate enlists. A soldier with peptic ulcer is of no value from a military point of view. Rather, he is a liability. He might, as a civilian, be of use in an occupation more suited to his capabilities. The importance of peptic ulcer from a pension aspect is, of course, self-evident.

A.G.N.

Editorial Comments

David Low, M.D., F.R.C.S.(C)

We regret to have to record the death of Dr. David Low, of Regina, which occurred on March 9, 1941.

Dr. Low was a Past-president of our Association (1925-1926) and held office at the Regina and Victoria meetings. This latter gathering was notable in that many enterprises of interest to medical men were broached and some were advanced a stage—foundation work which was well conceived, and well carried out, conducing greatly to the usefulness of our Association in subsequent years. Dr. Low was active in all that pertained to our welfare. He was particularly interested in the establishment of the Royal College of Physicians and Surgeons of Canada, and, as chairman of the Association's committee on the subject, was very active in making the proposal an actuality in 1927. He held, and rightly, that an examining body of this nature would be of great value in maintaining and indeed enhancing the standards of medical education in Canada. As an "elder statesman" in his city, he was looked up to for guidance, and was identified with many good works, notably the establishment of a modern hospital and the campaign against cancer. He has left a good record behind him and will be greatly missed. A.G.N.

War Medicine*

The first number of a new journal is before us. While it is a "new journal" it is not just "another journal". Its *raison d'être* is sufficient and its appearance timely.

A number of journals on war and aviation medicine are, of course, well known, but this one is welcome as it covers a much wider field than the others and bids fair to acquaint us with all phases of the medical and administrative war effort in the United States. The new journal is edited by the Committee on Information, National Research Council, in collaboration with the American Medical Association. Dr. Morris Fishbein is Chief Editor.

It will be admitted by all that the problems which arise in connection with the medical training and care of troops on land and sea and in the air are speedily becoming highly specialized and that the average doctor does not know and cannot be expected to know as yet all the points that make for greater efficiency in the service which he renders. His job is primarily to save life, and the wider his knowledge, the more efficient his work. It was recognized that co-operation was required in deciding upon the standardization of medical procedures and in the securing of adequate personnel, and, at the same time, that such efforts should be adequately reported. The Committee selected to publicize these efforts is composed of specialists in their various fields. It is hoped to develop a bank of information concerning physicians available for the Army in all its branches, for the Navy, and for industry and public health work, in particular. The table of contents for this first number is as follows.

Industrial Hygiene and the Navy in National Defence, E. W. Brown; Benzedrine Sulphate, A. C. Ivy and L. R. Krasno; Aviation Medicine in the United States Navy, F. Ceres; March Fracture, P. L. Moore and A. N. Bracher. Various Official Statements; Abstracts from Current Literature; Book Reviews.

This journal promises to be of use to a widening circle and deserves a cordial reception.

A.G.N.

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Men and Books

PARACELSUS*

BY E. P. SCARLETT

Calgary

I.

I appreciate very deeply the honour of being invited to speak to the Academy on the occasion of its annual historical night. It is always a pleasure to return to one's Alma Mater, to revive, "clad in the sober russet of middle life", the emotions and hopes of bright-coloured student days, and to ponder that eternal delightful enigma of all university men—What is it about one's university that colours the whole of the rest of life? It is a particular pleasure to re-visit this Academy, for here as a student I first discovered that modern colossus of learning, a medical library. I remember how in those blessed hours of student life, the long afternoons off, I struggled through medical books and periodicals, looking for simplicity and truth in medicine, and how bewildered I was when I failed to find them. I still use this library, through the kindly offices of Miss Poole, and, alas! I must confess that I still struggle through the books that come to me from this medical Alexandria of the east, and in my western fastness I am still at times bewildered and still as often as not fail in the quest for simplicity and truth in medicine. Nevertheless it gives me pleasure to speak here tonight if only in a small measure to pay homage to the spirit and traditions of this Academy and its library.

Over the doorway of the library in a certain quiet cathedral city in England is this inscription ΨΥΧΗΣ ΙΑΤΡΕΙΟΝ which in the vernacular may be rendered "The Dispensary of the Soul". This has always seemed to me an ideal motto for the physician's library. It blends the historical and the scientific spirit in that humanism which is the inner essence and the glory of our craft. I commend it to this library.

* * *

The late Sir Walter Raleigh wrote thus of the Renaissance:

> "That great movement of the mind of man brought with it the exhilaration of an untried freedom and the zest of unlimited experiment; but it took the human soul from its station in a balanced and rounded scheme of things, to deliver it over to every kind of danger and excess. . . . From his servant's estate in the great polity [of Catholic theology], man was released by the Renaissance, and became his own master in chaos, free to design and build and inhabit for himself. The enormous nature of the task, which after three centuries is still hardly begun, did not at first oppress him; he was like a child out of school, trying his strength and resource in all kinds of fantastic and extravagant attempts."

The man whom we are to consider this evening was, to use Raleigh's fine phrase, "a master in chaos". It is precisely because Paracelsus was like a child out of school and because of his "fantastic and extravagant" thought and speech that his name has come down to us today. But he was agonized by many of the same issues as ours today, living as he did in that disturbed and disillusioning period when the Renaissance passed over into the Reformation and the religious wars. He lived during a very significant turning of the ways in Europe, much as we are experiencing in our own time. It is fitting then that we should call him to mind in this four hundredth year from his death.

I fully realize that at the present moment, when it is so difficult to think of anything but of what is and what will be, circumstances debar us from practising that rarest and most valuable of the intellectual virtues, a true detachment. We have virtually been forced to give up thinking about the things that most truly concern us; we cannot proceed, for we are engaged in a struggle that is all-consuming. In the rapid whirl of events we have seen with our own eyes the apparent shipwreck of a morality and a religion in which, for all our scepticism, we obscurely trusted. We have watched a whole social order disappear into the deeps. We have watched with numbed senses the visible and material symbols of the past blown into dust. We are in the worst situation that the British people has had to face since the Dark Ages. We may have been thoughtless sentimentalists before the disaster; we are now cast as heroes in a tragedy. On such a scene for some one to come along and wish to discuss the figure of a man of four hundred years ago seems like presumption and futility. The speaker is apt to be regarded either as a Lucretian spectator of the misery of man or as a foolish idle dreamer.

And yet these very circumstances, with the world again in turmoil, should heighten our interest in Paracelsus who acted as a kind of catalytic agent upon the conflicting elements in a disturbed civilization. The great historical revolt which began in his time is still working itself out. We cannot escape from our past and least of all from those fundamentals with which the Renaissance period was concerned. As F. S. Oliver, one of the great political thinkers of our time, has written:

> "Our obligation to the sixteenth and eighteenth centuries is not cancelled or diminished because the nineteenth, wearied by a struggle that was nearly fatal, fell asleep and awoke again to find itself in a heaven of material prosperity which it mistook during fifty years for the millenium. We are still burdened with the honour of the stewardship. The nature of our duty has changed, but the duty itself is plain."

* An address delivered at the Stated Meeting, Library and Historical Night, Academy of Medicine, Toronto, January 7, 1941, in commemoration of the 400th anniversary of his death, September 24, 1541.

Our generation, I think, is at last engaged in the full and arduous discharge of that duty.

But you say that Paracelsus is at best a dusty tiresome figure. To the intellect of our time wild figures of his type seem to be the very crown and flower of futility; they are collectors of straws, and, for all their violence, misers of dust. And besides, Paracelsus was a philosopher, and "how tiresome are the one-eyed philosophies!" Above all he was mediæval! I may gently counter that Paracelsus is too often passed off with that word "mediæval" which among us has come to be used as a term of abuse. To be mediæval is not to be cast into outer darkness. We moderns are too prone to underrate the mediæval vision and sneer at the Schoolmen. But even if Paracelsus was essentially a man of the mediæval period, like certain other rebellious spirits, he liked to warm himself at fantastic fires, and on occasion he blundered into the speech of modern empiricism.

The first thing to do in the consideration of a complex and versatile genius is, if possible, to separate the man and his "legend", for every great man has his legend, the result of the impact of his personality on his time. In the case of Paracelsus this is an imperative but profoundly difficult task. He has always been and still is a semi-legendary figure. A mass of literature clusters round his name. Dark legends have hung cobwebs round the essential figure of the man. In sharp contrast to the qualities of his contemporaries—the superb detachment of Leonardo and the sombre passion of Michelangelo—he is a strangely mixed character behind whose swaggering periods of speech broods a mind which takes a dark pleasure in shattering the established forms of the time. The result has been that he has achieved a strange renown.

Now critical opinion must deal with this phenomenon. To be worth anything medical history must be more than the pious celebration of some ancient benefactor of our craft, a sort of sentimental ancestor worship. It is pleasant to record that medical historians have been busy with the separating of myth from fact in the life of Paracelsus. Not until the last century was he given his due place in medical history. To the work of many German scholars, and in particular to the monumental labours of that master of the historical craft, Karl Sudhoff, we are indebted for a better understanding of the personality and accomplishments of the eccentric genius who was Paracelsus.

I trust that I shall have due respect for these materials, and not slip into the besetting sin of so many modern impressionistic biographers. Their regard for the historical verities recalls the experience of a friend of mine who, while walking on one of the roads near Lexington, read a sign posted on a tree in the front yard of a farm-house. The sign read: "This is the original house at which Paul Revere would have stopped if he had ridden this way."

* * *

The life of Paracelsus swings through the glowing orbit of wayward genius. We shall plot it briefly, keeping in mind that everything concerning this man has been disputed at some time or another. He was born on December 7, 1493, in Einsiedeln, Switzerland, a village near the city of Zurich, which at the time was part of the German confederacy. So far as we know, he was an only child. His father, William Bombast von Hohenheim, an amiable, scholarly and respected burgher, was the physician of the village. His mother, of the family of Ochsner, belonged to a local religious sect, and was not, as is so often stated, the matron of the hospital. Doctor Bombast was a descendant of an old and celebrated family called of Hohenheim after their ancient residence, a castle in the vicinity of Stuttgart. He was his son's companion and instructor, and from him the boy learned as well the rudiments of alchemy, surgery and medicine. When the lad was nine years of age, the family removed to Villach where his father was the physician until his death. In the town there was a school founded by the Fuggers, of Augsburg, owners of lead mines, and here overseers and analysts were trained for the mines. In this school and in the mines and its laboratories Paracelsus gained his first interest in chemistry. The details of his formal schooling are obscure. He probably obtained his college education at Basel. We know that he received instruction from the celebrated Johan Trimethius, abbot of Wurzburg, one of the greatest living exponents of magic, alchemy and astrology, knowledge which was the basis of the dominant occultism in his later work.

Paracelsus is usually introduced with a list of names like a resounding roll of trumpets—Aureolus Philippus Theophrastus von Hohenheim, Paracelsus, Helvetius Eremita, and other extravagant variations. Such flourishes are the visible evidence of the legends which surround the man; a word or two is necessary to resolve this fantastic jumble. He was christened Theophrastus after the famous philosopher, the disciple of Aristotle. His parents may have given him the name Aureolus, a term often linked with the original Theophrastus, and Philippus may have been added at baptism to supply the customary saint's name, but neither of these names was ever used by Paracelsus himself. Bombast (not Bombastus), as we have seen, was the family name, and its connection with Paracelsus did not inspire the modern meaning of the word. Our term "bombast" is derived from an ancient word for cheap cotton used for stuffing, and hence by analogy has come to be employed for inflated or pompous speech. The name "Paracelsus" was adopted by the boy himself during his student years as was the custom of the time. Students travelling about to universities tended to take Greek or Latin names, as their own foreign

proper names were difficult to pronounce. The real surname of Erasmus, for example, was Gerhardt. In this manner Paracelsus came by his name, and inasmuch as it was chosen when he was a young student, it is unlikely that he interpreted it as meaning *beyond or superior to Celsus,* the great Roman medical writer, but rather gave the construction *beside Celsus,* which reflects the pride of the student entering the learned profession of medicine. The other names in his title are nicknames added by posterity. In the few authentic specimens of his handwriting, Paracelsus signs himself: Theophrastus, Theophrastus Paracelsus, or Theophrastus von Hohenheim.

Pascal has said that most of the evils of life arise from "man's being unable to sit still in a room". Whether for good or evil, when he was barely twenty, Paracelsus embarked on a career of travel, or possibly it might be described more correctly as years of wandering. The ferment of the Renaissance was working in him. Browning in his poem, with this idea in mind, has the fervent young Paracelsus exclaim:

> "I go to prove my soul!
> I see my way as birds their trackless way.
> I shall arrive! what time, what circuit first,
> I ask not: but unless God send his hail
> Or blinding fire-balls, sleet or stifling snow,
> In some time, His good time, I shall arrive:
> He guides me and the bird. In His good time!"

He served in campaigns as army surgeon in Denmark, Italy and Belgium, visited England, Portugal and France. Like so many Swiss mercenaries of the time, he took part in wars in the East and was certainly in Constantinople. Later he was an army surgeon in wars in the service of Venice (1521-1525). Like that earlier vagabond-scholar of genius, Villon, he sought the company of the lowliest type and particularly those versed in occult lore. There is no positive evidence that he ever received the degree of Doctor of Medicine, although it seems unlikely that he could have held his later posts had he not done so. When he was attacked by his opponents for this roving life, he replied with a magnificent defense of wandering: "A physician must be a traveler. . . If one will know many diseases he must wander also. . . Does not travel give more knowledge than sitting behind the stove? . . . Those who hug the fireplace wear silks and golden chains, those who wander are scarce able to pay for their homespun. . . For this will I bear witness respecting nature; he who will investigate her ways *must travel her books with his feet.*"

In the year 1526, at the age of thirty-two, Paracelsus returned to Germany. He had gained great experience, and soon attracted attention as an original physician. But his methods rapidly aroused hostility in conventional quarters, and he comments: "I pleased no one but the sick whom I cured". In appearance he was unusually small, very delicately built, was beardless, possessed a powerful nose and a sensitive mouth, and had a high, thin voice. Dr. Bernhardt Aschner says he was "not over 150 cm. high, had no attraction towards the female sex, and was of a very choleric and emotional temperament." Later he became more fleshy, his face puffy and smooth if we are to judge from portraits; at the last he was a prematurely old, thin, bitter man, preserving only the defiant, far-seeing appearance of the eyes.

In 1526 he was residing in Basel, where he treated some famous patients, notably Frobenius, the distinguished book publisher, and Erasmus, the greatest scholar and humanist of the time. He was appointed city physician, a position which carried with it the functions of a professorship in medicine, and now for the first time he moves to the centre of the historical stage as the born rebel. The following letter in Latin was placarded on the door of the University of Basel announcing his lectures.

> "Theophrastus Bombast von Hohenheim, a hermetic doctor and professor of both medicines. Whereas of all disciples, medicine only as being a certain divine gift, is praised with the honourable title and name of necessity, by the testimony of sacred writ and profane also. We intend to purge and cleanse it from the barbarous and grievous errors now successfully exercising it. We do not bind ourselves to any precepts of the ancients, but such as are evidently true. For who knows not that most of the doctors of this age have grossly erred to the exceeding hazard of the sick, in obstinately adhering to the sayings of Hippocrates, Galen, Avicenna, just as if they had been so many tripods or oracles from which it is unlawful to depart a finger's breadth. These authors make us brave doctors, but not physicians. For it is not title, nor eloquence, nor reading, nor many books, (though these things are ornaments) that make physicians, but an excellent and deep knowledge of things mysterious which is worth all the rest. The rhetorician learns to speak eloquently and persuade the judge, but the physician knows the kinds, the causes and the symptoms of affairs, and by piercing sight and industry to administer medicines rightly, and to heal who can be healed. Know then that I, being invited by the large stipend of Basle, do for two hours spare daily, publicly interpret, with accurate diligence my books, both of active and inspective medicine, to the great profit and advantage of my hearers. Wherefore, honest readers, if the mysteries of this apollinean art are delightful enough to any of you, and you covet thoroughly to learn in a short time, whatever pertains to this discipline, come to us at once at Basle, and you shall find other and greater things than I can describe in these few lines. But that my intention may appear more clearly to the studious, I am not ashamed to say that we do not all agree with the ancients in attributing all diseases to complexions and humors, for that is an error which has prevented doctors from reaching the truths as to diseases in their days. Let this as shown through a lattice suffice for today, but do not decide rashly until you have heard Theophrastus. Fare ye well and take in good part this our effort toward reformation in medicine.
>
> MDXXVII June, Basle.

Such statements and his bold divergence from the accepted doctrines and practice of the established medical schools at once aroused fierce opposition. To these offences he added the audacious heresy of teaching in the vernacular German rather than in the customary Latin tongue. With his irritable temper and love of conflict Paracelsus carried the battle to his op-

ponents. In a characteristic gesture he showed his breach with traditional authority by throwing into the students' bonfire on St. John's Day celebration, the most revered authority of the medical world of that time, the *Canon* of Avicenna. To the Galenical medical world this was the equivalent of the burning of the papal bull by Martin Luther. The battle was joined and the inevitable crisis arrived. When a prominent citizen of Basel, Canon Lichtenfels, whom he had cured, refused to pay his fee, Paracelsus sued him. The court ruled against Paracelsus, whereupon he denounced the courts and judges with such violence that he was forced to flee Basel.

Browning in his "Paracelsus" has him describe his Basel period in vivid words:

"Just so long as I was pleased
To play off the mere antics of my art,
Fantastic gambols leading to no end,
I got huge praise. . . . There they flocked,
Poor devils, jostling, swearing and perspiring,
Till the walls rang again; and all for me!
. . . I spoke out.
Forthwith a mighty squadron, in disgust,
Filed off — 'The sifted chaff of the sack', I said,
Redoubling my endeavours to secure
The rest. When lo! one man had tarried so long
Only to ascertain if I supported
This tenet of his, or that; . . . The other worthy
Discovered divers verses of St. John,
Which read successively, refreshed the soul,
But, muttered backwards, cured the gout, the stone,
The colic, and what not. Quid multa? The end
Was a clear class-room, and a quiet leer
From grave folk, and a sour reproachful glance
From those in chief, who, cap in hand, installed
The new professor scarce a year before.
. . . . Good night to Basil, then!
But fast as I proposed to rid the tribe
Of my obnoxious back, I could not spare them
The pleasure of a parting kick."

This parting kick is to be found in his book, the *Paragranum* which is a flaming outburst against slavery to the past and an indictment of the "abandoned academic Bacchantes who bear the name of doctor". It was not printed during his life. In its pages are passages of caustic eloquence, including the following which has become famous:

"Follow after me — not I after you — Ye after me, Avicenna, Galen, Rhasis, Montagnana, Mesue and ye others. After me and not I after you — ye of Paris, ye of Montpellier, ye of Swabia, ye of Meissen, ye of Cologna, ye of Vienna, and those who are on the Danube and the Rhine, ye islands of the sea — thou Italia, thou Dalmatia, thou Athens, thou Greece, thou Arabia, thou Israelita, after me and not I after you, — there will none of you remain in the furthest corner on whom the dogs will not turn. I shall be monarch and mine will be the monarchy."

He denounced the apothecaries and their "grievance".

"The apothecaries are my enemies because I will not empty their boxes. My recipes are simple and do not call for forty or fifty ingredients."

So, breathing defiance to the faculties and the profession, Paracelsus left Basel in 1528 after a residence of less than two years. For the remaining thirteen years of his life he was the lonely wanderer, a voice crying in the wilderness. He was driven from city to city, sometimes by restlessness, more often by bitter persecution. He devoted his time to practice, but more especially to writing treatises upon medicine, surgery, chemistry, philosophy and theology, almost all of which were refused publication in his day through the censorship of the entrenched Galenist medical authorities. It is the old story of the man and his message. These for the most part were years of fluctuating fortune, and at times of grinding poverty. We find him in Nuremberg in 1529 endeavouring to publish certain works. We get a glimpse of him in St. Gallen about 1533 in the entry of a diary of a citizen of the time: "Theophrastus is most laborious, he sleeps little, without undressing, throws himself, booted and spurred, on the bed for some three hours, and ceaselessly writes."

In 1534 he is to be seen entering Innsbruck in the Austrian Tyrol in poverty and rags. He seems to have retained, however, a considerable popular reputation. He ranged over the fields of medicine and mystical philosophy and astrology, even indulging, as was the custom of the time, in occasional prognostications of political and other events. Possibly on account of his eminence in the secret arts of alchemy and astrology, he was at length invited by the Prince Palatine, Duke Ernst of Bavaria, to the city of Salzburg where he seems finally to have found some security and a measure of peace. Here he died on the twenty-fourth of September, 1541. His last will and testament, written three days before death, has been preserved. None of the theories of the cause of his death are quite satisfactory. If one may judge from drawings made of him during the last two or three years of life, he suffered from some constitutional disease, as he had the appearance of advanced age.

He died in the faith of the church many of whose doctrines he had so savagely denounced. Rebel as he was, he still retained allegiance to the Catholic faith and ritual which had gathered unto itself so much of the richness and symbolism of the past. Like Browning's prelate, he was content in the end to lie where he could

"Hear the blessed mutter of the Mass,
And see God made and eaten all day long."

He was buried in the graveyard of St. Sebastian in Salzburg. At the base of his monument is the following inscription which, in translation from the Latin, reads:

"Here is buried Philippus Theophrastus, distinguished doctor of medicine, who with wonderful art cured dire wounds, leprosy, gout, dropsy and other contagious diseases of the body, and who gave to the poor the goods which he obtained and accumulated. In the year of our Lord 1541, the 24th of September, he exchanged life for death."

(To be continued)

Association Notes

THE SEVENTY-SECOND ANNUAL MEETING

of the

Canadian Medical Association

TO BE HELD IN WINNIPEG, JUNE 23, 24, 25, 26, 27, 1941

Convention Headquarters—Royal Alexandra Hotel

President - - - DR. DUNCAN GRAHAM, Toronto
President-Elect - - DR. GORDON S. FAHRNI, Winnipeg
General Secretary - - DR. T. C. ROUTLEY, Toronto

A Message from the President-Elect

Eleven years have passed since the Canadian Medical Association met conjointly with the British Medical Association in Winnipeg in 1930. Manitoba's turn to entertain the Dominion medical organization has come again—had it come in Peace Time, how happy we would have been! Last year a few weeks before the Annual Meeting in Toronto in June, when France was capitulating, there developed a strong current of opinion among a few that the meeting should be cancelled or, failing this, reduced to one of executive sessions only. Your Executive did not agree and the whole program was carried out as planned. The registration of physicians was the highest on record excepting only the conjoint meeting of the British Medical Association and the Canadian Medical Association in Winnipeg, August, 1930. The experience of last year has strengthened the hand of your Executive Committee and the Local Committee on Arrangements in their decision to proceed with the Annual Meeting in its usual form.

The Scientific Sessions are to be held on June 25th, 26th and 27th. Round-table Conferences from 9 to 10 o'clock introduce the program each morning and the General Sessions continue from 10.15 to 12.00 o'clock. The Sectional Meetings are convened each afternoon at 2 o'clock.

The General Council meets the first two days of the week, and the Annual Meetings of the Saskatchewan and Manitoba Divisions are scheduled for Tuesday afternoon, June 24th.

The profession of Manitoba are keenly conscious of the generous gesture of the Saskatchewan Division in moving their Annual Meeting this year to Winnipeg, and it is our hope that the large delegation that we are expecting from that Province will have no reason to regret their kind co-operation.

In addition to the Annual General Meeting Wednesday evening, a variety of entertainment is planned for all visiting physicians and their wives.

His Honour, the Lieutenant-Governor, and Mrs. McWilliams, in their gracious spirit of co-operation, are planning a Garden Party at Government House.

On behalf of the wives of the physicians of Manitoba may I state that they hope to have the pleasure of entertaining many wives of physicians from Halifax to Victoria.

The medical profession of Manitoba extends to the profession of each of the other eight provinces a hearty invitation to our meeting next June.

GORDON S. FAHRNI,
President-Elect.

Plans for the Seventy-second Annual Meeting, to be held in Winnipeg during the week of June 23rd next, are progressing most satisfactorily.

The Central Program Committee, under the Chairmanship of Dr. Duncan Graham, with valuable aid from the Local Program Committee in Winnipeg, has arranged a scientific program which should attract a large attendance.

General Council will meet on Monday and Tuesday.

On Tuesday afternoon both the Manitoba and Saskatchewan Divisions of the Association will hold their annual meetings.

The fourth annual conference of Medical Secretaries will be held on Monday evening.

The Canadian Medical Protective Association will hold its Annual Meeting at the close of the luncheon on Friday.

On Tuesday evening, members of General Council will be dinner guests of their Manitoba hosts.

Round-Table Conferences, instituted so successfully two years ago, will be continued this year on the mornings of Wednesday, Thursday and Friday, from nine to ten o'clock.

General Sessions will be held on Wednesday, Thursday and Friday mornings from 10.15 o'clock until 12.00 noon.

The various sections will hold their meetings on the afternoons of Wednesday, Thursday and Friday.

The Annual General Meeting will be held on Wednesday night.

Once again, as at the Toronto meeting, Thursday night has been given over to a dinner meeting under the auspices of the **Committee on Medical Economics**, of which Dr. Wallace Wilson, of Vancouver, is the Chairman.

Golfers are reminded that the Golf Tournament will be held all day Tuesday, when play for the beautiful Ontario Cup and other prizes will take place.

All the meetings will be held in the Royal Alexandra Hotel. The management has very kindly placed at our disposal the entire facilities of the hotel, thus affording splendid accommodation for all our requirements.

The Ladies have prepared an excellent program of entertainment for the visiting Ladies, full particulars of which will appear in the next issue of the *Journal*.

COMMITTEE ON ARRANGEMENTS

Chairman
THE PRESIDENT-ELECT, DR. G. S. FAHRNI
General Secretary
DR. T. C. ROUTLEY, TORONTO
Local Honorary Secretary
DR. M. J. ORMEROD

Chairmen and Secretaries of Committees

BADGES AND SIGNS—DR. A. BLONDAL, *Chairman.*
DR. L. A. SIGURDSON, *Secretary.*

COMMERCIAL EXHIBITS—DR. E. H. ALEXANDER, *Chairman.*
DR. H. MEDOVY, *Secretary.*

ENTERTAINMENT—DR. H. D. KITCHEN, *Chairman.*
DR. A. M. GOODWIN, *Secretary.*

GOLF—DR. G. L. ADAMSON, *Chairman.*
DR. I. O. FRYER, *Secretary.*

HOUSING AND EQUIPMENT—DR. J. M. MCEACHERN, *Chairman.*
DR. K. C. MCGIBBON, *Secretary.*

PUBLICITY—DR. W. F. ABBOTT, *Chairman.*
DR. F. G. ALLISON, *Secretary.*

REGISTRATION—DR. W. E. CAMPBELL, *Chairman.*
DR. EMMET DWYER, *Secretary.*

SCIENTIFIC EXHIBITS—DR. SARA MELTZER, *Chairman.*
DR. H. V. RICE, *Secretary.*

TRANSPORTATION—DR. M. R. MACCHARLES, *Chairman.*
DR. B. R. MOONEY, *Secretary.*

FINANCE—DR. F. G. MCGUINNESS, *Chairman.*
DR. W. G. BEATON, *Secretary.*

LIAISON WITH LADIES' COMMITTEE—DR. P. H. T. THORLAKSON, *Chairman.*
DR. B. D. BEST, *Secretary.*

Chairmen and Secretaries of Sections

ANÆSTHESIA—DR. D. C. AIKENHEAD, *Chairman.*
DR. D. G. REVELL, *Secretary.*

DERMATOLOGY—DR. A. M. DAVIDSON, *Chairman.*
DR. GEO. BROCK, *Secretary.*

MEDICINE—DR. J. D. ADAMSON, *Chairman.*
DR. D. S. MCEWEN, *Secretary.*

OBSTETRICS AND GYNÆCOLOGY—DR. J. D. MCQUEEN, *Chairman.*
DR. C. R. RICE, *Secretary.*

OPHTHALMOLOGY AND OTOLARYNGOLOGY—DR. E. J. WASHINGTON, *Chairman.*
DR. F. A. MACNEIL, *Secretary.*

PÆDIATRICS—DR. GORDON CHOWN, *Chairman.*
DR. HAROLD POPHAM, *Secretary.*

RADIOLOGY—DR. DIGBY WHEELER, *Chairman.*
DR. R. A. MACPHERSON, *Secretary.*

SURGERY—DR. O. S. WAUGH, *Chairman.*
DR. S. G. HERBERT, *Secretary.*

UROLOGY—DR. H. D. MORSE, *Chairman.*
DR. D. SWARTZ, *Secretary.*

HISTORICAL MEDICINE—DR. ROSS MITCHELL, *Chairman.*
PROF. I. MACLAREN THOMPSON, *Secretary.*

MILITARY MEDICINE—COLONEL P. G. BELL, *Chairman.*
LIEUT.-COLONEL T. E. HOLLAND, *Secretary.*

Local Program Committee

Chairman—DEAN A. T. MATHERS
Secretary—DR. C. W. BURNS

Drs. D. C. Aikenhead, A. M. Davidson, J. D. Adamson, J. D. McQueen, E. J. Washington, Gordon Chown, Digby Wheeler, O. S. Waugh, H. D. Morse, Ross Mitchell and Colonel P. G. Bell.

Local Advisory Committee

Chairman—DR. G. S. FAHRNI, PRESIDENT-ELECT
Hon. Secretary—DR. M. J. ORMEROD

Dr. E. L. Ross, President, Manitoba Medical Association; Dr. H. D. Kitchen, Vice-President, Manitoba Medical Association; Dr. Digby Wheeler, President, Winnipeg Medical Society; Dr. J. S. McInnes, President, College of Physicians and Surgeons of Manitoba; Dr. A. T. Mathers, Dean of Faculty of Medicine, University of Manitoba; Dr. O. C. Trainor, Manitoba representative on Canadian Medical Association Executive Committee; Dr. J. D. Adamson, Professor of Medicine, University of Manitoba; Dr. A. F. Menzies, Southern District; Dr. H. O. McDiarmid, Central and Western Districts; Dr. R. E. Dicks, Northern part of Province.

Ladies' Committee

Convener—MRS. G. S. FAHRNI

Mrs. M. J. Ormerod, Mrs. A. W. S. Hay, Mrs. H. D. Kitchen, Mrs. Digby Wheeler, Mrs. J. S. McInnes, Mrs. A. T. Mathers, Mrs. O. C. Trainor, Mrs. J. D. Adamson, Mrs. A. F. Menzies, Mrs. H. O. McDiarmid, Mrs. R. E. Dicks, Mrs. E. L. Ross, Mrs. P. H. T. Thorlakson.

GENERAL SESSIONS

Speakers and Subjects as Arranged to Date

Valedictory Address by the President
Dr. Duncan Graham, Toronto.

Dr. William F. Braasch, Rochester, Minn.
The surgical kidney as a factor with hypertension.

Dr. Charles Hunter, Winnipeg
Dizziness from the internist's standpoint.

Dr. F. W. Jackson, Winnipeg
Some observations on maternal care.

Dr. A. F. Menzies, Morden
Post-war medical problems.

Dr. Gavin Miller, Montreal
Recent advances in the surgical approach to carcinoma of the large bowel and rectum.

Dr. Rustin McIntosh, New York
Jaundice.

Dr. Kenneth G. McKenzie, and
Dr. E. H. Botterell, Toronto
The common neurological syndromes produced by pressure from extrusion of an intervertebral disc. (Illustrated by coloured film).

Dr. G. E. Richards, Toronto
Ten years' progress in the radiotherapy of oral cancer. Present methods and present results.

The Osler Lecture.
Speaker to be announced.

Dr. Wallace Wilson, Vancouver
Whither Medicine!

Dr. Ralph M. Tovell, and
Dr. Curtiss B. Hickcox, Hartford, Conn.
The present status of cyclopropane.

SECTIONAL MEETINGS

Section of Anæsthesia

Dr. D. H. Huggins, Winnipeg
Avertin in neuro-surgery.

Dr. D. G. Revell, Winnipeg
Ether, the all-purpose anæsthetic.

Dr. H. V. Rice, Winnipeg
Newer concepts of anæsthetic physiology.

Dr. C. H. Robson, Toronto
Anæsthesia for children (illustrated by coloured film).

Dr. R. M. Tovell, and
Dr. A. W. Friend, Hartford, Conn.
The control of physical hazards of anæsthesia.

Symposium on Spinal Anæsthesia

Dr. Byron R. Burwash, Saskatoon
Analeptics.

Dr. I. H. Davidson, Winnipeg
Pre-medication.

Dr. K. E. Hollis, Toronto
Indications and contraindications.

Dr. H. J. Shields, Toronto
Physiology.

Dr. G. D. Stanley, Calgary
Sequelæ in intraspinal anæsthesia.

Dr. Norman S. Clark, Toronto
Agents.

Section of Historical Medicine

Dr. William Boyd, Toronto
The evolution of medical science.

Dr. J. H. Elliott, Toronto
Osler's class at the Toronto School of Medicine.

Dr. W. A. Gardner, Winnipeg
A voice from St. Helena.

Dr. J. A. Gunn, Winnipeg
Ambroise Paré as a military surgeon.

Dr. J. C. Hossack, Winnipeg
History of the plague.

Dr. D. S. Macnab, Calgary
Hugh Owen Thomas.

Dr. A. G. Nicholls, Montreal
Herba panacea.

Dr. N. R. Rawson, Winnipeg
William Farr, founder of vital statistics.

Dr. D. G. Revell, Edmonton
The first twenty-five years of anatomy teaching in Alberta.

Section of Medicine

Dr. G. F. Amyot, Victoria
Public health and the private practice of medicine.

Dr. Eldon M. Boyd, Kingston
Expectoration, expectorants and cough medicines.

Dr. William Boyd, Toronto
Changing views regarding pyelonephritis.

Dr. F. T. Cadham, Winnipeg
Vaccine therapy in atrophic arthritis.

Dr. A. T. Cameron, Winnipeg
Blood plasma; proteins; — their clinical significance.

Dr. R. J. Collins, East Saint John
Problems arising in rehabilitation schemes for the tuberculous.

Dr. J. H. Geddes, London
What is colitis?

Dr. A. A. Fletcher, and
Dr. Wallace Graham, Toronto
Gold therapy in chronic arthritis.

Dr. F. C. Heal, Moose Jaw
The management of common disorders of cardiac rhythm.

Dr. E. S. Mills, and
Dr. E. S. Murray, Montreal
The relative value of the various sulphonamide drugs in the treatment of acute respiratory infections including pneumonia.

Dr. J. M. McEachern, Winnipeg
Coronary disease in Manitoba.

Dr. D. S. McEwen, Winnipeg
Upper respiratory infection in general practice.

Dr. Harris McPhedran, Toronto
Cardiovascular disease associated with toxic goitre.

Dr. Trevor Owen, Toronto
Fatigue, rest and exercise.

Dr. T. A. Pincock, Brandon
Transitions in psychiatry.

Dr. John W. Scott, Edmonton
The natural history of migraine.

Dr. S. E. C. Turvey, Vancouver
Asymptomatic neurosyphilis.

Section of Military Medicine

Symposium—Medical aspects of casualties returning from overseas.

Introduction—

Lieut.-Colonel A. M. Davidson, President, Standing Medical Board, No. 10 Detachment, R.C.A.M.C., M.D. 10.

Section of Military Medicine—*Continued*

Medical Cases—

Captain H. S. Atkinson, No. 10 Detachment, R.C.A.M.C.

Dr. J. D. Adamson, Medical Staff, D.P.&N.H., Winnipeg.

Surgical Cases—

Lieut.-Colonel T. E. Holland, R.C.A.M.C., Officer Commanding, Fort Osborne Military Hospital, M.D. 10.

Dr. J. A. Gunn, Surgeon, D.P.&N.H., Winnipeg.

Eye, Ear, Nose and Throat Cases—

Major H. G. Grieve, No. 10 Detachment, R.C.A.M.C.

Problems of Army Hygiene

Major M. R. Elliott, District Hygiene Officer, No. 10 Detachment, R.C.A.M.C.

Special problems of the R.C.A.F. Medical Officer

Wing-Commander G. E. Hall, Ottawa.

Section of Obstetrics and Gynæcology

Dr. L. C. Conn, and
Dr. J. R. Vant, Edmonton
Uterine prolapse.

Dr. Léon Gérin-Lajoie, Montreal
Contribution to the surgery of the pre-sacral nerve in gynæcological ailments.

Dr. W. S. Holmes, Saskatoon
Induction of labour—indications, methods and dangers.

Dr. P. J. Kearns, Montreal
Anatomical changes in the lower uterine segment in pregnancy and labour.

Dr. John Mann, Toronto
Toxæmia of pregnancy; present day classification; etiology and treatment.

Dr. F. G. McGuinness, Winnipeg
The obstetrical significance of intra-cranial injury of the newborn, based on 300 autopsies.

Dr. A. B. Nash, Victoria
Treatment of acute and chronic salpingitis.

Dr. N. W. Philpott, Montreal
Anæsthesia and analgesia in obstetrics with particular reference to the use of local anæsthesia.

Dr. C. R. Rice, Winnipeg
Disturbances of menstrual function in tuberculous patients.

Section of Ophthalmology

Dr. K. J. Austmann, Winnipeg
Glaucoma.

Dr. D. M. Genoff, Winnipeg
Senile cataract.

Section of Ophthalmology—*Continued*

Dr. H. O. McDiarmid, Brandon
Interocular tumours.

Dr. F. D. McKenty, Winnipeg
The results of tarsectomy and a simplification of the technique.

Dr. Fred T. Tooke, and
Dr. John V. Nicholls, Montreal
The incidence and character of hæmorrhages occurring in the retina in diabetes.

Section of Otolaryngology

Dr. G. W. Fletcher, Winnipeg
Tumours of the larynx—diagnosis and treatment.

Dr. Keith Hutchison, Montreal
Acute otitic meningitis; chemotherapy advances.

Dr. Gregor McGregor, Toronto
Bronchoscopy — a safeguard against diagnostic errors.

Dr. George Tremble, Montreal
Irrigation of the sphenoid sinuses — a safe and simple method (illustrated by coloured film).

Dr. E. J. Washington, Winnipeg
Intracranial complications of otogenous origin with review of cases.

Clinical presentation of cases at the General Hospital and St. Boniface Hospital.

Section of Pædiatrics

Dr. A. R. Birt, Winnipeg
Troublesome skin diseases in infancy and childhood.

Dr. Alan Brown, Toronto
Diarrhœa.

Dr. Alfred Deacon, Winnipeg
Rehabilitation of poliomyelitis cases.

Dr. Donald Fraser, Toronto
Prophylactic immunization in children.

Dr. U. J. Gareau, Regina
Acrodynia.

Dr. Alton Goldbloom, and
Dr. N. W. McLellan, Montreal
Staphylococcal septicæmia — prognosis and treatment.

Dr. K. B. Leslie, Winnipeg
Medication before and after anæsthesia in children.

Dr. L. M. Lindsay, and
Dr. F. W. Wiglesworth, Montreal
Report of two cases of purpura fulminans.

Dr. H. S. Little, London
Chemotherapy of meningococcic meningitis.

Dr. Rustin McIntosh, New York
Nephritis.

Dr. Graham Ross, Montreal
The use of vitamin K in pædiatric practice, with special reference to the newborn period.

Section of Pædiatrics—*Continued*

Dr. R. R. Struthers, and
Dr. H. L. Bacal, Montreal.
The significance of rheumatic nodules in childhood.

Dr. F. F. Tisdall, Toronto
War and post-war problems regarding childhood nutrition.

Section of Radiology

Dr. L. J. Carter, Brandon
Radiological examination of the terminal ileum and proximal colons—a twenty-five year résumé.

Dr. A. D. Irvine, Edmonton
Coarctation of the aorta, radiologically considered.

Dr. Hervé Lacharité, Montreal
Osteochondritis dissecans.

Dr. W. H. McGuffin, Calgary
Radiological evidence as a diagnostic aid in diseases of the heart.

Dr. Carleton B. Peirce, and
Dr. D. L. McRae, Montreal
Bronchography in pulmonary disease of undetermined cause.

Symposium on Carcinoma of the Cervix
Anatomy—
Professor I. Maclaren Thompson, Winnipeg.
Pathology—
Dr. Sara Meltzer, Winnipeg.
Radium—
Dr. Ethlyn Trapp, Vancouver.
X-radiation—
Dr. A. W. Blair, Regina.
Metastasis and management—
Dr. B. R. Mooney, Winnipeg.
Complications following radiation treatment in carcinoma of the cervix—
Dr. W. G. Cosbie, Toronto.

Section of Surgery

Dr. A. C. Abbott, Winnipeg
Inguinal hernia with special reference to recurrence.

Dr. C. W. Burns, Winnipeg
Surgical management of traumatic abdomen.

Dr. Walter G. Carscadden, Toronto
Injuries of the hand.

Dr. W. F. Gillespie, Edmonton
The treatment of perianal abscess and fistula.

Section of Surgery—*Continued.*

Dr. Chas. W. Harris, Toronto
Injuries about the ankle joint.

Dr. Robert C. Laird, Toronto
The diagnosis and treatment of bronchiectasis.

Dr. R. K. Magee, Peterborough
Subphrenic abscess.

Dr. Herbert Meltzer, Ninette
181 cases of thoracoplasty.

Dr. H. F. Moseley, Montreal
Shoulder pain.

Dr. M. R. MacCharles, Winnipeg
Causes of poor results in biliary tract surgery.

Dr. Lorne H. McConnell, Saskatoon
Epilepsy — analysis of the results of 91 craniotomies.

Dr. J. S. McEachern, Calgary
Some surgical problems arising from developmental errors.

Dr. O. W. Niemeier, Hamilton
Obstructive jaundice.

Dr. George Ramsay, London
Anterior poliomyelitis; observations on recovery rate of paralyzed muscles.

Dr. Fulton Risdon, Toronto
The present status of the treatment of hare lip and cleft palate deformities.

Dr. Dudley E. Ross, and
Dr. J. H. Palmer, Montreal
The surgical treatment of patent ductus arteriosus.

Section of Urology

Dr. E. D. Busby, London
Present status of chemotherapy in urinary infections.

Dr. W. F. Braasch, Rochester, Minn.
Prognosis in non-surgical bilateral renal tuberculosis.

Dr. Earl Hall, Vancouver
Carcinoma of the penis.

Dr. J. C. McClelland, Toronto
Anuria.

Dr. Frank S. Patch, and
Dr. J. T. Codnere, Montreal
Treatment of hydronephrosis secondary to aberrant renal vessels.

Dr. Robin Pearse, Toronto
Lipofibrosacromata of the kidney.

Dr. Frederick Pilcher, Calgary
Transurethral prostatic resection.

Section of Urology—*Continued*

Dr. Emerson Smith, Montreal
Experiences with interstitial cystitis

Dr. C. B. Stewart, Winnipeg
Persistent Wolffian duct—report of cases.

Dr. G. N. Tucker, Edmonton
Recumbency urolithiasis.

Medical Economics

Municipal doctor system in Saskatchewan
Dr. R. O. Davison, Regina.

What is an adequate medical service?
Dr. E. S. Moorhead, Winnipeg.

Some of the weaknesses observed in health insurance plans which have been studied.
Dr. T. C. Routley, Toronto.

Summary
Mr. Hugh H. Wolfenden, Toronto, Consulting Actuary of the Association.

ROUND-TABLE CONFERENCES

Subjects and Chairmen

Medicine

Migraine
Dr. H. D. Kitchen, Winnipeg.

Normal blood pressure variations
Dr. L. G. Bell, Winnipeg, *Chairman*
Dr. J. D. Adamson, Winnipeg
Squadron Leader F. A. L. Mathewson, Regina
Dr. Alex. McLean, Rochester.

Prevention of common cold
Dr. William Wood, Winnipeg.

Obstetrics and Gynæcology

Management of ante- and post-partum hæmorrhage
Dr. Ross Mitchell, Winnipeg.

Carcinoma of the uterus
Dr. J. D. McQueen, Winnipeg.

Ophthalmology

Orthoptic treatment of strabismus
Dr. F. A. McNeil, Winnipeg.

Corneal lesions
Dr. J. T. Cruise, Winnipeg.

Otolaryngology

Upper respiratory infections
Dr. Robert Black, Winnipeg, *Chairman*
Dr. A. Leishman, Winnipeg
Dr. F. D. McKenty, Winnipeg.

Pædiatrics

Chronic cough in childhood
Dr. O. J. Day, Winnipeg.

Genito-urinary infections in childhood
Dr. C. B. Stewart, Winnipeg.

Surgery

Fractures
Dr. A. Gibson, Winnipeg.

Acute appendicitis
Dr. P. H. T. Thorlakson, Winnipeg.

Tumour clinic
Dr. Daniel Nicholson, Winnipeg, *Chairman*
Dr. George T. Pack, New York, visiting consultant.
1. Cancer of the breast—case presentation.
2. Tumours in the neck (where primary site was not obvious). Report of final diagnoses in the last 100 cases at the Winnipeg General Hospital Tumour Clinic.
   Carotid body tumour—case presentation.
3. Neurogenic sarcoma—case presentation.

Urology

Bladder tumours
Dr. H. D. Morse, Winnipeg.

The present status of endocrine therapy in urology
Dr. C. B. Stewart, Winnipeg.

TRANSPORTATION

Identification certificates may be obtained from the office of the General Secretary, 184 College Street, Toronto. These certificates entitle the purchaser to round-trip fare at one and one-third of the adult normal one-way first class or coach fare, plus 25 cents. Tickets are good going and returning via same route, or going via one authorized route and returning via any other authorized route. Return limit, thirty days, in addition to date of sale. Passengers must reach original starting point not later than midnight of final return limit.

Dates of sale:

From Ontario (Port Arthur, Armstrong and West), Manitoba Saskatchewan, Alberta and British Columbia—June 17th to 23rd (both dates inclusive).

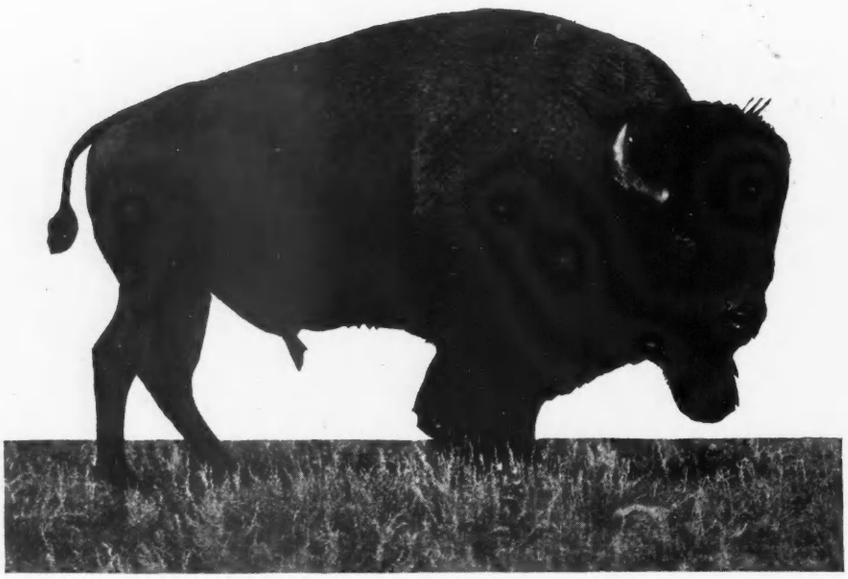
From Ontario (east of Port Arthur and Armstrong), Quebec, New Brunswick, Nova Scotia, and Prince Edward Island, June 16th to 24th (both dates inclusive).

WINNIPEG HOTELS

DAILY RATES — EUROPEAN PLAN

	Single room without bath	*Single room with bath*	*Double room without bath*	*Double room with bath*
Clarendon Hotel	$1.50	$2.00	$2.00	$3.00
Fort Garry Hotel	3.50	5.00	5.00	7.00
Mall Hotel	2.50	3.00	4.00	5.00
Marlborough Hotel	2.00	3.00	3.00	4.50
Royal Alexandra Hotel	3.50	5.00	5.00	7.00
St. Charles Hotel	1.50	2.25	2.50	4.00
St. Regis Hotel	1.50	2.50	2.50	3.50

MANITOBA AND ITS CAPITAL



Pierre Gaultier de la Verendrye, accompanied by two sons, arrived at the Forks of the Red and Assiniboine Rivers on September 24, 1738, the first white men to see the site of the future city of Winnipeg. They found there only ten Cree huts and two chiefs. After a few days they continued up the Assiniboine River to what is now Portage la Prairie, but were soon followed by one of the partners who, in October, 1738, started the erection of Fort Rouge on the south bank of the Assiniboine River, now part of Winnipeg. La Verendrye and his party continued their explorations westward and into what is now the states of North and South Dakota and Montana, in the hope and belief that that land might contain a water route to the Pacific Ocean. He died on December 6, 1749.

The Selkirk Settlement.—Lord Selkirk was one of the shareholders of the Hudson's Bay Company, and, to carry out his colonization plans, he made arrangements whereby he obtained a land grant of 116,000 square miles on the banks of the Red and Assiniboine Rivers from this Company. The first party of his settlers from the north of Scotland and the Orkney Islands arrived on the banks of the Red River at what is now Kildonan on August 30, 1812, travelling in small sailing boats to York Factory on Hudson Bay, thence via the Hayes River, Lake Winnipeg, and the Red River to their destination. The descendants of these settlers are very proud of their heritage, and, today, are numbered amongst our most highly respected citizens.

Upper Fort Garry.—What is now the City of Winnipeg had within its territory in the early Red River days many forts or fur-trading posts, including Fort Rouge, Fort Gibraltar and Fort Douglas. Chief among them in point of importance and historic significance was Fort Garry, headquarters of the Hudson's Bay Company. It was erected in 1822 on the site of what was formerly Fort Gibraltar. In 1835 it was re-built with many alterations and extensions. It was unfortunate that it occupied ground that blocked an important thoroughfare, Main Street south, which necessitated its final demolition in 1882.

Lower Fort Garry.—Twenty miles north of Winnipeg on the banks of the Red River is Lower Fort Garry, a fort whose bastions, loopholed walls, as well as many of its interior structures, are built of Manitoba stone quarried nearby. To the Selkirk Settlers it was known as Fort Garry, but the fur traders, Hudson's Bay Company officers and servants, the voyageurs and Indians, knew it and talked familiary about it as the Stone Fort. It is the only stone fort of the early fur traders in Canada still intact and in a state of perfect preservation, and through the generosity of the Hudson's Bay Company will go down to posterity as a monument of the early Red River days. Building was commenced in 1831, and completed with walls and bastions in 1839. The Hudson's Bay Company have leased it to the Motor Country Club, and members and visitors alike enjoy its golf course and hospitality.

GATEWAY TO UPPER FORT GARRY, WINNIPEG

Winnipeg.—In 1870 the population of the City of Winnipeg was 215, today, over 224,000, (Greater Winnipeg over 318,000). It was incorporated in 1873, with a population of 1,869, and is the capital city of Manitoba and one of Canada's four metropolitan centres. Its altitude above sea level is 760 feet. Winnipeg is an important manufacturing centre, and the gateway to rich and extensive mining areas. It has also become the greatest grain centre on the North American continent, the financial, commercial, wholesale and manufacturing centre of the Middle West, and the educational centre of the Province. It has over sixty hotels, forty-two beautiful public parks and squares, eighteen golf courses. The city has wide and well paved thoroughfares, beautiful boulevards and residential streets. Its three main thoroughfares, 132 feet wide, are the widest on the continent.

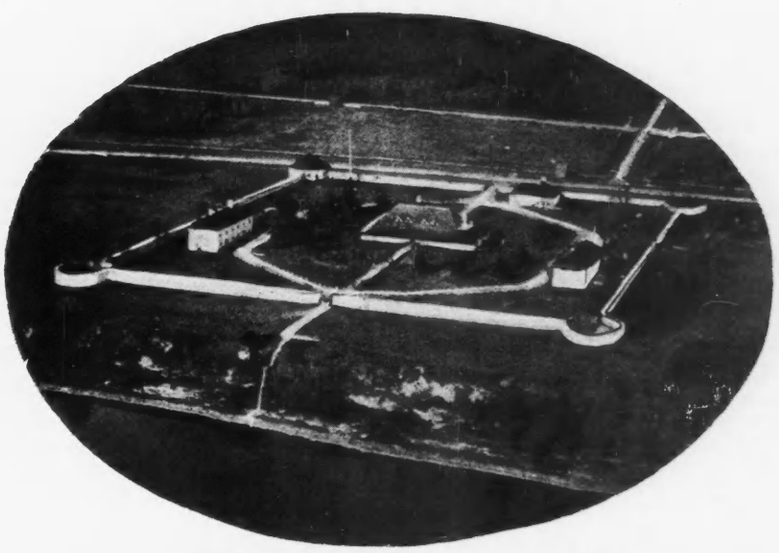
The city is noted for many fine public buildings and beautiful homes; having the largest cash grain market in the world; the cheapest hydro-electric light and power on the continent; the largest individually owned railway yards in the world; and the largest Musical Festival in the British Empire.

Winnipeg's principal shopping district extends along Portage Avenue and Main Street, two splendid business thoroughfares noted for their great width. Here the visitor will find large departmental stores, presenting merchandise from the four corners of the earth. In the district will also be found splendid moving picture houses, vaudeville and legitimate stage theatres, restaurants, etc. The larger stores maintain travel bureaux for the convenience of visitors.

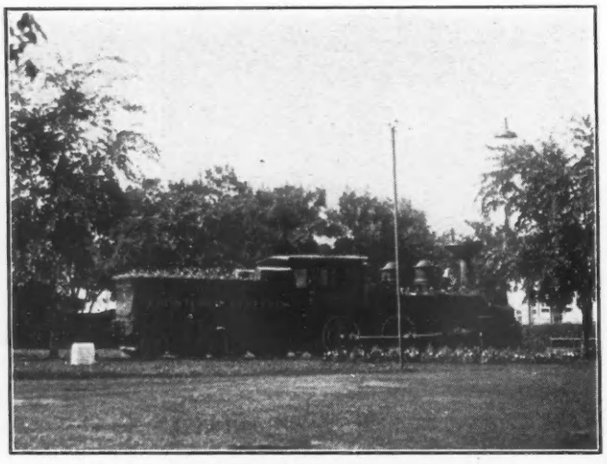
The Parliament Building, one of the finest and largest structures of its kind on the continent, is built of native Tyndall stone, and is a splendid monument to the progressive public-spirited people of Winnipeg and Manitoba.

The Auditorium, also built of the same native stone, is the finest building of its kind in Canada. It is a civic venture and cost over one million dollars.

Stevenson Airport, one of the most modern on the continent, affords air travel to the south, east and west, as well as the mining fields in northern Manitoba.



LOWER FORT GARRY FROM THE AIR



FIRST ENGINE IN WINNIPEG REGION

Winnipeg, in the very centre of Canada, is also a focal point for railway and bus transportation in all directions.

CKY Radio Station is one of the most powerful in Canada, with modern studios. Visitors are welcome to see through the studios on personally conducted tours.

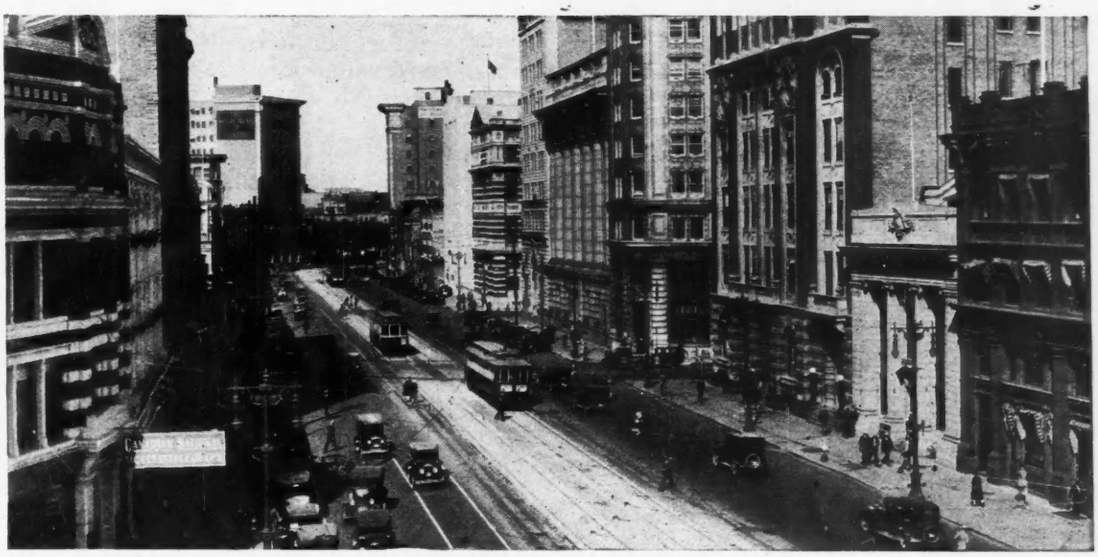
Fort Prince of Wales.—Was erected of wood by the early Hudson's Bay Company traders some five miles up the Churchill River in the year 1688. A second fort, also of wood, was built in 1718, but the depredations of French rivals of the Company caused them to construct a more formidable one of stone in 1733, the materials for which were secured nearby. The walls were originally designed to be forty-two feet thick, but were reduced to twenty-five feet. In 1782, when manned by a small force, the French disembarked four hundred troops on the shore of Churchill Bay, and, being greatly outnumbered, the Governor surrendered this great stronghold to the French without firing a shot in its defence. The Fort was looted, and for two days an attempt was made to demolish it, which was only partially successful, for some of the walls resisted every effort, and are today all that remain of this historic fort.

Churchill.—In August, 1927, after extensive investigations, it was decided that Churchill should be the terminus of the Hudson Bay Railway instead of Port Nelson, chiefly on account of its better harbour facilities. By April, 1929, steel had been laid all the way to Churchill, and a temporary wharf and a few other buildings were erected. In 1928 ships began to arrive with timber, coal and other supplies, also instruments, masts and equipment for a wireless station. Today it is a modern harbour port, with huge storage grain elevators, stockyards to accommodate twenty car loads of cattle, and other up-to-date improvements. From this port a goodly portion of Western Canada's grain and livestock is shipped to European markets.

PARLIAMENT BUILDINGS, WINNIPEG

RIDING MOUNTAIN NATIONAL PARK

One hundred and seventy-three miles northwest of Winnipeg over all-weather highways; 2,200 feet above sea level. Luxuriant forests, crystal clear lakes, wild animal and bird life. Every facility for the comfort and enjoyment of the visitor. Hotels, lodges, cabin camps and camping grounds. Horseback riding, golf, tennis and other sports.



DOWN-TOWN WINNIPEG

THE WHITESHELL PROVINCIAL PARK

One hundred miles east of Winnipeg over hard-surfaced highways. Over one thousand square miles of natural scenic beauty. It contains some two hundred lakes and numerous streams of crystal clearness. Good fishing, hunting, and canoe trips. Cabin camps and camping grounds.

INTERNATIONAL PEACE GARDEN

A scenic area of 2,200 acres in Manitoba and North Dakota, with lodge and cabin camp accommodation. Cabin camps are also available at nearby Lake Killarney.

LAKE WINNIPEG

Fifty miles north of Winnipeg over hard-surfaced highways. Several fine resorts, including Winnipeg Beach, Sans Souci (Matlock), Grand Beach and Victoria Beach. Swimming, boating, golfing and other sports. Hotels, cabin camps, and camping grounds. Weekly boat trips on this lake from Winnipeg to Historic Norway House, one of the oldest Hudson's Bay Company trading posts in the west.

THE BEGINNING OF A PORTAGE

MINAKI, ONTARIO

One hundred and fourteen miles east of Winnipeg on the main line of the Canadian National Railways, and at the north end of the beautiful Lake of the Woods country. Good fishing, hunting, swimming, boating and golfing. Fine lodge accommodation.

KENORA, ONTARIO

On hundred and twenty-six miles east of Winnipeg on the main line of the Canadian Pacific Railway, 145 miles over hard surfaced highways. Over eight thousand population. Good fishing, hunting, swimming, boating, sailing, and golfing. Good hotel and cabin camp accommodation. Daily boat service between Kenora and Minaki during the summer season.

By-Laws Governing Membership in and Attendance at Annual Meetings of the Canadian Medical Association

Now that all Provincial Medical Associations have become Divisions of the Canadian Medical Association the By-Laws for Divisions become applicable to Canada as a whole. It is well, therefore, that all members, both of the parent Association and of Divisions, clearly understand the basis of membership and annual meeting arrangements, including registration.

With that end in view, the following extracts from the By-Laws of the Canadian Medical Association are published.

CHAPTER I — DIVISIONS

"A Branch Association may become a Division as outlined in Article V of the Constitution and enjoy all the rights and privileges of a Division in the following manner:

1. By intimating to The Canadian Medical Association in writing that it desires to become a Division.
2. By agreeing to amend where necessary its Constitution and By-Laws, to place them in harmony with the Constitution and By-Laws of this Association.
3. By agreeing to collect from all of its Divisional Members who desire to be members of The Canadian Medical Association such annual fee as may from time to time be set for membership and remit same to this Association.
4. By agreeing to take such steps as seem proper to the Division to increase membership in The Association."

CHAPTER II, SECTION 9

REGISTRATION AT MEETINGS

"No member shall take part in the proceedings of the Canadian Medical Association, or in the proceedings of any of the sections thereof, or attend any part of the meeting until he has properly registered. Only members and invited guests are eligible to register and attend an annual meeting."

CHAPTER IV — SECTION 2

ARRANGEMENTS FOR ANNUAL MEETINGS

"When the Canadian Medical Association meets in any province where there is a Branch Association or Division the meeting of that Branch Association or Division for that year shall be for business purposes only. The local arrangements shall be under the direction of the Executive Committee of The Canadian Medical Association, which may enlist the assistance of the Branch Association or Division or one of its component societies. The Canadian Medical Association assumes full control of the proceedings of the meeting and of all financial obligations save entertainment."

MEMBERSHIP

Medical practitioners in good standing resident in Canada may become members of the Canadian Medical Association in one of two ways:

By-Laws, Chapter II, Section 1 — Ordinary Members

Every member in good standing in a Division shall be automatically an Ordinary Member of the C.M.A. on payment of the annual fee as levied by the General Council.

By-Laws, Chapter II, Section 2 — Members-at-Large

Any graduate in medicine residing in Canada who is not a member of a Division may be accepted as a member of the C.M.A. provided that, with his application, a certificate of approval from the Executive body of the Division in which the applicant resides, be furnished to the General Secretary. In the case of an applicant residing in Canada in a territory beyond the jurisdiction of a Division the applicant must be endorsed by two members of the C.M.A. Such members shall be designated Members-at-Large and shall pay the annual fee as levied by the General Council.

CONCLUSION

The foregoing extracts from the By-Laws, read in conjunction, make it clear that, applicable to all of Canada save that portion which is outside the jurisdiction of any province, all members of the Canadian Medical Association, whether ordinary members or members-at-large, must have the sanction of the Division in which the member resides.

Only members of the Canadian Medical Association may register at a meeting of the Canadian Medical Association and attend sessions.

The annual meeting of the Division which may be held at the same time and place as the annual meeting of the Canadian Medical Association is for business purposes only; and, as this meeting is entirely separate and distinct from the annual meeting of the Canadian Medical Association, membership in the Division only qualifies for registration to attend the business meeting of the Division.

Amendment to Constitution and By-Laws

In order to make provision for alternates for elected members of the Executive Committee, the Committee on Constitution and By-Laws will move the following amendment to the By-Laws at the next meeting of General Council which will be held in Winnipeg on June 23 and 24, 1941. This Notice of Amendment is published in the *Journal* in compliance with the By-Laws (Chap. XII, Sect. 2).

Chapter VI, Section 2 — Duties of Nominating Committee.—Paragraphs 2 and 3 now read as follows:

(2) Nominations of an Executive Committee which, in addition to those who are members *ex officio* (See Chapter VIII, Section 4), shall consist of thirteen members drawn from General Council and geographically distributed as follows: three shall be resident in each province in which an office of The Association is located and one shall be resident in each of the other provinces.
At its session, the Nominating Committee may receive in writing a Division's official nomination of the candidate or candidates for representation on the Executive Committee to which the Division is entitled. In the event of an official nomination being rejected by the Nominating Committee the reasons for such action shall be incorporated in its report to General Council.

(3) *Rules of Procedure:* The Committee shall be called to order by the President as Chairman of the Committee. In the absence of the President the General Secretary shall convene the Committee and request the Committee to select, by open vote, the Chairman. The Committee shall then proceed to carry out its duties by open vote. In case of a tie vote the Chairman shall have the casting vote in addition to the vote to which he is entitled as a member of the Committee. When called for, the report of the Committee shall be presented to the General Council by the General Secretary.

The above-mentioned paragraphs shall be amended to read as follows:

(2) Nomination of an Executive Committee which, in addition to those who are members *ex officio* (See Chapter VIII, Section 4) shall consist of thirteen members drawn from General Council and geographically distributed as follows: three shall be resident in each province in which an

office of The Association is located and one shall be resident in each of the other provinces.

(3) Nomination from members of General Council of *nine* alternates for the elected members of the Executive Committee. There shall be one alternate nominated from each province. The function of the alternates shall be to act in the place of an elected member of the Executive Committee who is absent because of death or illness or from cause acceptable to the President.

(4) At its session the Nominating Committee may receive in writing (1) each Divisions official nomination of the candidate or candidates for representation on the Executive Committee to which the Division is entitled, and also (2) each Division's official nomination of *one* alternate who will act in the absence by reason of death or illness or from cause acceptable to the President of the member or one of the members representing that Division. In the event of such an official nomination by a Division being rejected by the Nominating Committee the reasons for such action shall be incorporated in its report to General Council.

(5) Rules of Procedure — (unchanged except that paragraph is renumbered.)

The War

National War Services

Major-General L. R. LaFléche, National War Services, has sent in the following table of statistics relative to the medical examination of recruits which is valuable for record, as it conveys important information.

Number of men tabulated: 10,000.

			Per cent
Category	A	6,905	69.05
	B1	904	9.04
	B2	236	2.36
	C1	293	2.93
	C2	383	3.83
	D	112	1.12
	E	1,167	11.67
Canadian-born		9,672	96.72
British-born		175	1.75
Non-British-born		153	1.53

It will be noted that the total number of disabilities shown does not coincide with the total number of men examined. The explanation is that some men are free of any disability whilst others suffer from one or more.

Rheumatism	585	5.85
Tuberculosis	74	0.74
Bronchitis, asthma	563	5.63
Heart disease	257	2.57
Kidney, bladder	270	2.70
Stomach, intestinal	844	8.44
Rupture	442	4.42
Varicose veins	129	1.29
Foot trouble	836	8.36
Nasal trouble	634	6.34
Ear trouble	564	5.64
Eye disease	595	5.95
Fits	82	0.82
Mental and nervous	195	1.95
Syphilis	17	0.17
Gonorrhœa	130	1.30
Glasses	1,414	14.14
Previously rejected for military service	340	3.40
In receipt of pension	17	0.17
Wear dentures	352	3.52
Average height	5 ft. 7 in.	
Average weight	146.97 lbs.	

15th March, 1941.

R.C.A.M.C. Takes Over Red Cross Hospital at Taplow

The model hospital erected by the Canadian Red Cross at Taplow on the estate of Viscount and Viscountess Astor was officially turned over to the Royal Canadian Army Medical Corps last July. Originally planned as a 300-bed hospital, the buildings as finally completed will house twice that number in 15 wards. In view of the nature of the site it was decided to construct the hospital as a series of one story units placed parallel to each other along a central axis. It was also decided that brick and steel construction would be the best choice of structural material, considering the relative cost of materials, the war hazards, and the use to be made of the buildings. The buildings themselves cost some $590,000, with the equipment additional, a large proportion of the cost being specially contributed.

The hospital is now being operated by the staff of Number 5 General Hospital which is made up largely of the personnel from the Manitoba area. Colonel C. L. T. Arthur, of Winnipeg, is in command and the fifty Canadian nurses are under the direction of Miss Jean Machray who is the matron of the hospital. Lieut.-Col. Roy Richardson is in charge of surgery and Lieut.-Col. Charles Walton, of medicine.

At the opening ceremony the Rt. Hon. R. B. Bennett presented this fine hospital to the Canadian High Commissioner, Hon. Vincent Massey, who accepted it on behalf of the Canadian Government. It was then turned over to Colonel R. M. Luton, Senior Medical Officer of the C.A.S.F. in Great Britain. Colonel George Nasmith, Deputy Commissioner of the Canadian Red Cross in Great Britain, presided.

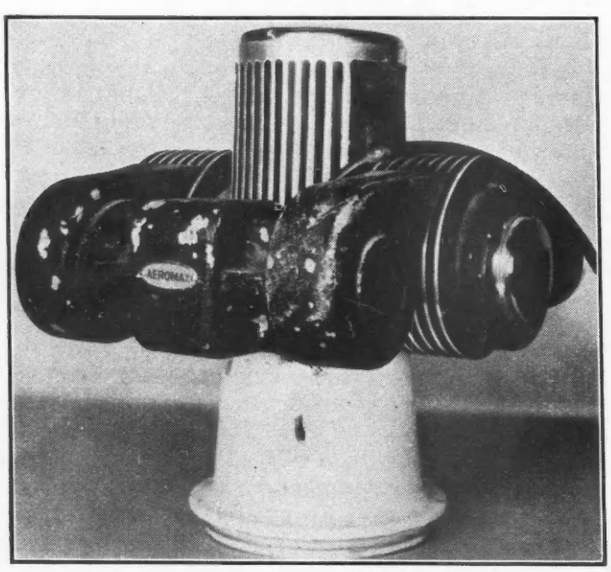
U.S. Health Unit and Liaison Officer

With the consent of the President of Harvard University, Dr. J. E. Gordon, who holds the Charles Wilder Chair of Preventive Medicine and Epidemiology at Harvard, has accepted Mr. Malcolm MacDonald's invitation to act as United States Liaison Officer with the Ministry of Health. Shortly after the outbreak of war Harvard University appointed a committee to consider how the university could contribute material or professional help to a cause closely concerned with its interests. The possible nature of this help was conceived in the broadest terms, with the suggestion that it might be in economics, medicine, sociology, public health, law, and perhaps other fields. Through an exchange of opinion between authorities of Harvard and colleagues in Great Britain it later became evident that help in the fields of public health and medicine was most clearly in point. As a consequence Harvard University made a formal offer to the Minister of Health, which Mr. MacDonald gratefully accepted, to equip and maintain in Great Britain a public health unit for the study and control of communicable disease. The purposes of the unit were defined as: (1) to lend material

aid to a friendly nation; (2) to investigate communicable disease under unusual military and civil conditions; (3) to obtain medical information of value to the national defence of America. The unit as originally conceived was to include a group of workers concerned with field studies in epidemiology and a laboratory for the study of associated problems. British authorities early pointed out the desirability of adding to this basic unit a well-equipped hospital for the clinical care and study of communicable disease. This addition became possible through the active co-operation of the American Red Cross, who agreed to build and transport to Great Britain a hospital of 125 beds. The final plans for the unit evolved from discussions between Prof. Gordon and the authorities of the Ministry of Health in London during August and September. Facilities and staff are provided for the study of communicable disease in the field, in the laboratory, and at the bedside. Prof. Gordon returned to America in the latter part of September to assemble staff, order equipment, and lay plans for the hospital. He left in London Dr. John R. Mote, assistant in epidemiology in the Department of Preventive Medicine, Harvard University, now acting as medical adviser to the American Red Cross Committee in London, to continue and complete local arrangements. Prof. Gordon has now returned here, and the first shipments of buildings and equipment are expected to arrive shortly. The headquarters of the unit will be in southwest England, with provision for a mobile team to serve more widely as need may arise. As U.S. Liaison Officer with the Ministry of Health, Prof. Gordon has an office in the Ministry, and is taken freely into the confidence of the Minister and the staff of the Department.—*Brit. M. J.*, 1941, 1: 249.

Damage to X-ray Apparatus from Bombing

The accompanying illustration shows a portable x-ray tube which has been subjected to "enemy action" in England. The mobile x-ray unit to which it belonged was almost completely destroyed but the tube was rescued. It was somewhat marked by its experience, as may be seen, but was still in good working order.



This tube, which was designed and made by the Machlett Laboratories in the United States, is an excellent example of the great improvements in modern x-ray design. The tube which used to be the most fragile element in an x-ray unit is now enclosed in an aluminium housing lined with lead and immersed in oil. These measures not only protect the operator from shock and burn, but help to cool the tubes and cushion it against jarring.

We understand that there are many such tubes in use in England.

A.R.P. in Germany

Air-raid precautions have been prominent in the minds of most citizens in this country, both lay and medical, for the last year or so. A long article by Professor Anschütz, of Kiel, gives an interesting glimpse of the medical side of A.R.P. in Germany. Apparently the German plan is to transport the wounded in ambulances and other vehicles to stations in which a good deal of treatment may be done. "Rettungsstellen" seem to correspond to casualty clearing stations rather than to our conception of first-aid posts. When the vehicle arrives an "energetic and experienced" medical officer enters it and selects the cases which shall be treated at the post, leaving the others undisturbed to be taken to hospital. The facilities for operation are by no means equal to those in hospital, but they are much greater than we regard as desirable in this country. He prepares those who are to remain for treatment in the dressing-room or theatre. His is therefore the most difficult task, perhaps the most responsible of all, and the author thinks that it should be undertaken by the chief officer of the station. Before even the first lorry arrives the station may be besieged by walking wounded, and the staff must never relax their vigilance in periods between raids. Instruments, gloves, and bandages must be ready in sterilized parcels, and the station ready to go instantly into action. He warns the staff against yielding to a temptation to detain particularly interesting cases; they occupy far too much time, during which the lighter cases pile up and congest the waiting-rooms. The relief of pain is an important part of first-aid, and he considers the best drug for this purpose to be the "S.E.E." mixture—scopolamine, eucodal, and ephetonine. A weak solution is injected intravenously until the patient becomes drowsy; with this procedure there is little risk of an overdose. With subcutaneous injection it is unsafe to give more than one ampoule. If the patient is badly shocked, small doses should be given at frequent intervals. Professor Anschütz reminds readers that to be prepared may not be everything, but it is a very large in-

gredient of success. The work of the station will be done under the public eye, and critics will abound; an adequate performance depends on every member of the staff being ready and doing his best. This counsel applies equally to our own organization. The German medical services are probably being tested already.—*Brit. M. J.*, 1940, **1**: 1025.

War Literature

ANNALS OF INTERNAL MEDICINE

Developments in Aviation Medicine, H. G. Armstrong, 1940, **13**: 2212.

ARCHIVES OF SURGERY

Improvement in Blood Transfusion Service, P. Hoxworth and C. Skinner, 1941, **42**: 480 and 498.

BRISTOL MEDICO-CHIRURGICAL JOURNAL

Head Injuries in Wartime, F. W. Willway, 1940, **57**: 91.

THE BRITISH MEDICAL JOURNAL

Some recent Air-raid Casualties, Margaret Ball and George Quist, 1941, **1**: 273.

Technique for Fastening a Casualty on an A.R.P. Stretcher with Triangular Bandages, 1941, **1**: 280.

Chemoprophylaxis of Gas Gangrene, 1941, **1**: 282.

Chemotherapy and Wound Infection (Society meeting), 1941, **1**: 288.

Depressive States in War, D. Curran and W. P. Mallinson, 1941, **1**: 305.

Treatment of Air-raid Casualties, P. H. Mitchiner, 1941, **1**: 309.

CANADIAN MEDICAL ASSOCIATION JOURNAL

Some Aspects of Aviation Medicine, R. W. Ryan and G. E. Hall, 1941, **44**: 227.

EDINBURGH MEDICAL JOURNAL

War and Skin Disease, G. H. Percival, 1941, **48**: 73.

THE LANCET

Overtime and Overtiring (leading article), 1941, **1**: 181.

Chemotherapy of Gas Gangrene: Material and Methods—experimental, J. McIntosh and F. R. Selbie, 1941, **1**: 240.

Elimination of Streptococci from Superficial Wounds by Sulfanilamide Powder, L. Colebrook, 1941, **1**: 271.

The Stretcher Patient Secured, 1941, **1**: 289.

N.Y. STATE JOURNAL OF MEDICINE

Medical Problems of Diving and Submarines, L. W. Johnson, 1940, **40**: 1065.

BOOKS AND PAMPHLETS

Surgery of Modern Warfare. Part I. Hamilton Bailey. 160 pp. E. & S. Livingston, Edin., 1940. Price 13s.

Industrial Hygiene, A. J. Lanza and J. A. Goldberg, Oxford University Press, London, 743 pp. Price 42s.

Health and Efficiency of Munition Workers, H. M. Vernon, Oxford University Press, London, 138 pp. Price 8/6.

Bulletin of War Medicine, 1941, No. 3 (very valuable). H. M. Stationery Office, York House, Kingsway, London W.C.2. Price 2/6 net.

Special Surgery in War Time. Edited by Sir Humphry Rolleston and Alan Moncrieff, Eyre Spottiswoode, London. Price 6s.

KING ARTHUR SPEAKS

I come again, my England, from the vale
Of Avalon, and stand upon the shore
Where once I ruled. I hear again the roar
Of Cornish waves, and in my shining mail
I listen through their thunder to the wail
Of wrongs I have but power to deplore.
A knight in armor is a force no more,
And few are left who seek the Holy Grail.
Since English hearts again have need of me
I cannot be at peace in Avalon;
But I, according to the prophecy,
Have come among them, as in days long gone,
And walk with them again the ancient road
They travel, to the glory of their God.

HARRIET D. RICHARDSON.

(Reprinted from the *New York Weekly Times*)

Medical Societies

The Regina and District Medical Society

Captain Douglas Taylor, of Montreal, addressed the April meeting of the Regina and District Medical Society on "Arthritis".

He said that arthritis is a whole family of diseases; there are at least twenty different kinds. The medical profession is to blame for the attitude of hopelessness. The teaching regarding rheumatic diseases is poor in Canada. In the United States $200,000,000 is spent on quacks each year for the treatment of these conditions. There are more of these cases than there are of tuberculosis, cancer and heart trouble put together. He showed slides illustrating various kinds of arthritis, also slides showing the use of plaster casts. In addition to casts he uses heat, gentle massage (no massage in acute states), good diet, iron and vitamins. Fat people are reduced.

Captain Taylor considered a certain Ontario centre where many arthritis patients go to have feet twisted, a blot on the medical history of Canada. He condemned the use of Crowe's vaccine in clear unmistakable terms. In fact he is dubious that vaccines have any value in arthritis. He also condemned "Ertron" and wished something could be done to stop the advertising that goes out about it. Ridiculously high doses of vitamin D came under his displeasure. He warned against missing *Brucella* in patients with joint trouble since 50,000 milch cows in Saskatchewan have given a positive test for Bang's disease. LILLIAN A. CHASE

The Royal College of Physicians and Surgeons of Canada

The eleventh Annual Meeting of the Royal College of Physicians and Surgeons of Canada was held in the Auditorium of the National Research Council Building, Ottawa, on Saturday, October 26, 1940. One hundred and forty-six Fellows registered.

At a meeting of the Council held in June, 1940, it was decided to create annual lectureships, two in English and one in the French language, and to present to these lecturers special diplomas at the Annual Meeting. The lecturers are to be known as "The 1940 Lecturer of The Royal College of Physicians", "The 1940 Lecturer of the Royal College of Surgeons" and "Conférencier du Collège Royal des Médecins et Chirurgiens pour l'année 1940" as the case may be; a primary presentation of the English lectures to be made at each annual meeting of the College. The lecture in the French language to be given at an appro-

priate meeting, not necessarily organized by the Royal College. It was furthermore provided by Council that the formal lectures given at the Annual Meeting might be repeated as secondary Royal College Lectures at some point east of Montreal and west of Toronto. The question of whether these secondary lectures should be given this year, for example in Halifax to the east and in Winnipeg or Vancouver to the west, was discussed and decided in the negative.

In accordance with the above resolution the following scientific program was presented.

A. H. Gordon, M.D., C.M., D.C.L., F.R.C.P. (C), Montreal, 1940 Lecturer. "Recent advances in medicine—etiology and therapy." Commentary by James Douglas Adamson, M.D., Winnipeg.

W. E. Gallie, M.D., F.R.C.S.(Eng.), F.R.C.S. (C), F.A.C.S., Toronto, 1940 Lecturer. "Recent advances in surgery—wound healing." Commentary by Wilfred Alan Curry, M.D., Halifax.

A lecture entitled "L'histoire de la transfusion" was given at the meeting of the French Congress at Three Rivers, P.Q., on Monday, September 9th, by Léo Errol Pariseau, M.D., D.P.H., D.Sc., F.R.C.P.(C), of Montreal.

After a short recess the Annual Business Meeting of the College was convened, with the President, Dr. Wilder G. Penfield in the Chair.

Dr. Albert LeSage, Vice-president, Division of Medicine, presented to the President the candidates qualified, by examination, to receive Fellowship in the Royal College of Physicians of Canada; Dr. Arthur Edwin Blackett, New Glasgow, N.S.; Dr. Walter Bethune Carruthers, Sarnia, Ont.

Dr. John A. Gunn, Vice-president, Division of Surgery, presented to the President the candidates qualified by examination to receive Fellowship in the Royal College of Surgeons of Canada: Dr. Frederick Douglas Ackman, Montreal; Dr. Gordon Charles Johnston, Vancouver; Dr. Neil MacDonald, Windsor, Ont.; Dr. Richard MacGregor Parsons, Red Deer, Alta.

Of nine applications for *Ad eundem* Fellowship two were acted upon favourably, and Fellowship in the Royal College of Surgeons of Canada was granted to the following: Dr. Robert Clarence Laird, B.A., M.S., F.R.C.S.(Eng.), Toronto; Dr. Donald Colin MacRae, F.R.C.S. (Edin.), Regina.

Lectureship Diplomas were awarded to: Dr. Alvah Hovey Gordon, 1940 Lecturer of the Royal College of Physicians of Canada; Dr. William Edward Gallie, 1940 Lecturer of the Royal College of Surgeons of Canada; Dr. Léo Errol Pariseau, Conférencier du Collège Royal des Médecins et Chirurgiens pour l'année 1940.

Honorary Fellowship in the Royal College of Physicians of Canada and Honorary Fellowship in the Royal College of Surgeons of Canada was conferred upon: The Right Honourable Alexander Augustus Frederick George, Earl of Athlone, K.G., P.C., G.C.B., G.C.M.G., G.C.V.O., D.S.O., A.D.C., Governor-General and Commander-in-Chief of the Dominion of Canada.

With the Fellows standing the names of those deceased during the year were read by the Honorary Secretary.

Physicians. — The Right Honourable Lord Tweedsmuir, February, 1940; Dr. J. J. Langlais, Trois Pistoles, November, 1939; Dr. A. H. W. Caulfeild, Toronto, May, 1940; Dr. J. F. Fotheringham, Toronto, May, 1940; Dr. J. G. FitzGerald, Toronto, June, 1940; Dr. A. J. Douglas, Winnipeg, June, 1940; Dr. F. G. Finley, Montreal, July, 1940; Dr. Maude E. Abbott, Montreal, September, 1940; Dr. W. B. Almon, Halifax, September, 1940.

Surgeons. — The Right Honourable Lord Tweedsmuir, February, 1940; Dr. W. H. Smith, Winnipeg, April, 1939; Dr. Gilbert Royce, Toronto, May, 1939; Dr. A. R. Campbell, Yarmouth, N.S., March, 1940; Dr. P. C. Dagneau, Quebec, July, 1940; Dr. J. McKenty, Winnipeg, August, 1940; Dr. F. Bertrand, Sherbrooke, P.Q., February, 1940.

A report of the activities of the Council during the year was presented by the President.

Meetings had been held in Toronto, on June 17th, and again in Ottawa (three sessions) at the time of the annual meeting.

The annual examinations were held as follows. Written examinations on September 30th, October 1st and October 2nd. Oral and clinical examinations took place in Edmonton on October 21st, and in Montreal on October 24th and 25th.

Of the thirty-two candidates who tried the Primary Examinations there were eight who took the French Examinations. There were no French candidates in the final examinations. The names of the successful candidates are as follows: Dr. Brock M. Fahrni, Winnipeg; Dr. John Wallace McNichol, Hamilton; Dr. Harold L. Richard, Edmonton; Dr. William Shandro, Vegreville, Alta.; Mr. Robert G. Bell, Toronto; Mr. Robert H. Cram, London; Mr. Robert W. Dingwall, Kingston; Mr. Armand Genest, Montreal; Mr. Robert Genest, Montreal; Mr. Jean Grignon, Montreal; Mr. George L. Ingham, Stratford, Ont.; Miss Madeliene Longtin, Saint Philippe, P.Q.; Mr. Gerard G. Lippert, Kitchener; Mr. Andre Mackay, Montreal; Miss Jeanne H. Montgomery, Toronto; Mr. Leonard G. Roussel, Ottawa; Mr. David B. Stark, Toronto; Mr. George C. Walsh, Montreal.

The following physicians and surgeons were admitted to Fellowship: Profs. Edmond Dubé, Gaston Lapierre, Emile Legrand, Paul Letondal, Albéric Marin, Roméo Pepin, Ernest Prud'homme, Louis P. Senécal, Sylvio Caron, Gustave Desrochers, Emile Fortier, Jean B. Jobin, Lucien LaRue, Joseph L. Petitclerc, Paul Garneau.

The following calendar for 1941 has been agreed to.

June meeting of Council, Winnipeg, Monday, June 23rd.

Annual Meeting, Ottawa, Saturday, October 25th.

Written examinations, Monday, September 29th; Tuesday, September 30th; Wednesday, October 1st.

Oral and clinical examinations, Montreal, Tuesday, October 21st and Wednesday, October 22nd. Toronto, Thursday, October 23rd and Friday, October 24th.

The Annual Dinner was held at the Chateau Laurier. His Excellency the Governor-General, was the guest of the College and addressed the Fellows after the dinner.

La société médicale des hôpitaux universitaires de Québec

Cette société tenait une assemblée, le 21 février, 1941, à l'Hôpital du St-Sacrement, Québec.

Suivent des résumés.

UN CAS DE FIBROME DU MAXILLAIRE INFÉRIEUR.—J. Paul Roger et J. M. Lemieux.

Le 22 octobre 1940, une malade agée de 23 ans, consulta pour une tuméfaction du maxillaire inférieur qui était apparue trois semaines auparavant. Une radiographie fut faite qui montra une image par soustraction qui comprenait presque toute la hauteur de la branche horizontale du maxillaire inférieur. On fit une résection partielle du maxillaire inférieur et l'examen anatomopathologique de la tumeur révéla qu'il s'agissait d'un ostéo-fibrome.

Les ostéo-fibromes sont des tumeurs plutôt exceptionnelles; au maxillaire inférieur où on les rencontre le plus fréquemment ils ne constituent que 3 pour cent de toutes les tumeurs.

On distingue des fibromes centraux et des fibromes périphériques; celui de cette malade était un fibrome central.

Les résultats opératoires furent excellents. La partie enlevés s'est reformée aux dépens du périoste et l'impotence est à peu près nulle.

Il y eut présentation de la patiente.

ANESTHÉSIE AU PENTOTHAL CHEZ UN HÉROÏNOMANE.—Adrien Paquet.

Nous avons eu l'occasion d'observer l'effet combiné des associations narcotiques en donnant du pentothal à un héroïnomane qui recevait 40 grs. d'héroine par jour. L'anesthésie a été parfaite avec une dose de pentothal ordinaire, soit 6 c.c. Pour obtenir ce résultat la vitesse d'injection du pentothal a été doublée: le malade a reçu une injection de la solution à 10 pour cent de pentothal, au rythme de 2 c.c. par cinq chiffres comptés par le malade en 5 secondes, la vitesse d'injection régulière étant de 1 c.c.

De cette observation se dégage les remarques suivantes: Il existerait une dose d'efficacité minima pour le pentothal, dose individuelle, variable avec les médications préliminaires et les anesthésiques de base. Pour obtenir cette dose d'efficacité minima la vitesse d'injection ne doit pas être trop lente sans quoi l'anesthésie sera imparfaite. Chez ce malade, la toxicité à l'héroïne ne semble pas avoir influencé la réceptivité aux barbituriques. Il est logique de croire que les associations anesthésiques augmentent l'anesthésie sans que s'additionnent les toxicités.

La localisation des centres de la narcose serait aux pédoncules cérébraux. Les anesthésiques pour produire la narcose doivent inhiber les pédoncules de façon directe, comme le pentothal, ou de façon indirecte, comme l'éther, qui agira d'abord sur l'écorce cérébrale pour donner la période d'excitation, avant d'obtenir l'anesthésie chirurgicale, par action secondaire et par dosage plus élevé sur les pédoncules cérébraux.

L'absence d'action du pentothal sur l'écorce cérébrale et son action directe sur les pédoncules expliqueraient l'absence de période d'excitation au cours de l'anesthésie au pentothal.

LARYNGITE CATARRHALE AIGUE ET CORPS ÉTRANGER.—Marcel Langlois.

L'observation présentée est celle d'un enfant d'un an qui a aspiré un corps étranger, en l'espèce une punaise de dessinateur à l'insu de ses parents et des médecins.

Les symptômes qu'a présentés l'enfant étaient ceux d'une trachéite avec bronchorrhée purulente. Elle était associée à une contracture douloureuse en episthotonos et une souffrance continuelle diurne et nocturne de la part de l'enfant. La présence d'un corps étranger a été involontairement révélé au cours d'un examen radiologique pulmonaire destiné à déceler une pneumopathie. L'aire radiologique a dépassé les régions habituelles considérées dans les examens pulmonaires et nous a permis d'apercevoir le corps étranger au niveau présumé du larynx. L'abcès pré-vertébral qui expliquait les symptômes, douleurs, contractures et bronchorrhée n'est qu'une complication nécessaire de la pénétration de ce corps étranger. Cette observation a le mérite d'illustrer qu'il ne faut pas toujours limiter les recherches radiographiques au territoire limité par la clinique.

CONSIDERATIONS SUR TROIS CAS DE MALADIE D'ADDISON.—R. Lemieux et A. Martel.

Des trois malades qui font l'objet de cette communication et qui ont présenté chacun une maladie d'Addison typique, deux moururent malgré une thérapeutique par l'hormone cortico-surrénale et la réchloruration. A l'autopsie on trouva dans les deux cas une tuberculose caséeuse des deux glandes surrénales.

Les signes humoraux que nous avons constatés chez ces trois malades ont présenté des variations souvent contradictoires. En général, dans la maladie d'Addison, les modifications de l'équilibre humoral sont constantes et elles permettent le dépistage précoce des états d'insuffisance surrénale fruste ou la confirmation d'un addisonisme douteux.

Ces modifications humorales portent sur le chlore, le sucre, le sodium, le potassium, le cholestérol, l'urée et le glutathion. La glycémie est habituellement basse. Mais plus encore que cette hypoglycémie isolée, l'hypersensibilité à l'insuline doit être considérée comme caractéristique de la maladie d'Addison. La concentration du chlore globulaire et plasmatique baisse considérablement, tandis que l'élimination de ce corps par les urines est augmentée. On note, en même temps, une baisse appréciable du taux du sodium et du calcium sanguins, ainsi que de la réserve alcaline. L'augmentation du potassium sérique est un phénomène constant chez les addisoniens. La suppression du chlorure de sodium de l'alimentation d'un addisonien ou l'augmentation de l'apport de potassium provoquent l'apparition de phénomènes graves. Cette restriction du Nacl, avec administration de potassium, est à la base des épreuves dont on se sert pour le diagnostic de la maladie d'Addison. On considère qu'une concentration du chlore plasmatique de moins de 121 mgm. par 100 c.c. et une concentration urinaire de plus de 225 mgm. de chlore par 100 c.c. sont fortement en faveur d'une maladie d'Addison. Une élévation de l'azotémie, un abaissement du taux du cholestérol sanguin et du glutathion, un abaissement du métabolisme basal ainsi que du taux d'élimination urinaire de la vitamine C, sont des constatations très fréquentes dans cette maladie.

Les principaux éléments du traitement sont: l'hormone cortico-surrénale, à doses élevées: 5 à 20 c.c. par jour. La réchloruration sous forme de chlorure de sodium per os ou de sérum hypertonique salé par voie veineuse. La vitamine C, à hautes doses: 1 gramme par jour, per os ou par voie intra-veineuse. Régime pauvre en potassium.

Winnipeg Medical Society

The program of the regular monthly meeting of the Winnipeg Medical Society on March 21st was contributed by the Medical History Section of the Society. Dr. J. C. Hossack gave a scholarly introduction, pointing out the value of medical history and showing how medical events had affected the course of history. Dr. W. A. Gardiner spoke on the "Edwin Smith Papyrus"; Dr. J. D. Adamson on "Sydenham"; and Dr. Ross Mitchell on "Organization of Medical Services in the Rebellion in 1885", illustrated with slides. ROSS MITCHELL

Abstracts from Current Literature

Medicine

The late Results of Artificial Pneumothorax in Pulmonary Tuberculosis. Clarke, B. R. and Erskine, S. L. W.: *Quart. J. Med.*, 1940, **9**: 323.

Artificial pneumothorax was applied to the treatment of 400 tuberculous patients at the Forster Green Hospital (Ireland) during the years 1925 to 1933 inclusive, and 99 per cent of the cases were followed up for a minimum period of five years. Ninety-seven per cent had tubercle bacilli in the sputum and 88 per cent showed x-ray evidence of cavitation. The youngest patient was 14 and the eldest 55 years of age, and there was approximately equal sex distribution. Satisfactory collapse was obtained in 33 per cent, partial collapse in 46 per cent, and no collapse in 21 per cent.

It was found that the good results of artificial pneumothorax were almost entirely limited to those cases in which a good collapse was obtained. The patients with an unsatisfactory collapse fared worse, from a mortality standpoint, than those in whom collapse could not be obtained, and the authors conclude that artificial pneumothorax should be discontinued as soon as it is evident that a good collapse is unattainable. Artificial pneumothorax was more successful, the earlier it was instituted after onset of illness (55 per cent within 6 months, 20 per cent after 12 months).

One hundred and eighty-one of the 400 patients had phrenic evulsion done on the same side as the pneumothorax (18 per cent of cases during the first five years of the series and 62 per cent during the final three years). The results were much improved during the final three years and this improvement was attributed to the phrenic evulsion. NORMAN S. SKINNER

Cancer of the Stomach. Gray, H. K.: *Proc. Staff Meet., Mayo Clinic*, 1941, **16**: 65.

La gravité du cancer de l'estomac a été bien démontrée par l'excellent travail de Livingston et Pack, qui démontre que la mortalité causée par le cancer de l'estomac est deux fois et demie plus élevée que la mortalité totale occasionnée par toutes les guerres auquelles ont participé les Etats-Unis. Le seul traitement curateur jusqu'à date d'aujourd'hui est l'intervention chirurgicale et la résection gastrique. Malheureusement il persiste chez le public et aussi chez plusieurs membres de la profession médicale une attitude de négligence à l'égard de *"symptomes gastriques persistants"* et une attitude d'attente "d'*histoire clinique dite classique*" qui fait faire le diagnostic lorsqu'il est trop tard.

Le cancer latent de l'estomac est heureusement rare et la plupart du temps hors de toute thérapeutique. L'enseignement à ce sujet doit être modifié et doit s'inspirer autant pour le médecin que pour le public, de principe suivant: La nécessité de consulter pour tout trouble digestif, quelque vague qu'il soit, ne répondant pas rapidement à la thérapeutique habituelle ou nécessitant constamment un traitement; de plus et ceci regarde spécialement le médecin, le devoir qu'a celui-ci de faire ou de demander des examens complets afin d'arriver à un diagnostic précis. D'après l'auteur un deuxième facteur de mortalité élevée par néoplasme gastrique est l'ignorance du fait suivant: "la malignité en puissance" d'un ulcère gastrique qui peut et dans une proportion assez importante subit un processus de dégénérescence maligne.

Le diagnostic clinique et radiologique est difficile et doit se baser sur les faits suivants: (1) la disparition de la douleur et des hémorragies cliniques ou microscopiques. (2) La disparition de la niche—signes sur lesquels Eusterman et Balfour ont insisté—semblent favoriser la bénignité d'une lésion. Mais il ne faut pas oublier que la "niche" peut paraître guérie radiologiquement même en présence d'une transformation maligne. C'est pourquoi l'auteur préconise la résection gastrique quand cela est possible chez les ulcéreux gastriques ou l'observation et le contrôle médical très sévère à l'hôpital. YVES CHAPUT

Surgery

The Surgical Treatment of Carcinoma of the Thoracic Œsophagus. Garlock, J. H.: *Surg., Gyn. & Obst.*, 1940, **70**: 556.

Ces cancers ne sont opérés surtout que depuis 4 ou 5 ans, le petit nombre des cas opérés, de 15 à 20, semble dû à la réputation de haute gravité de cette chirurgie. Jusqu'à récemment, considéré comme fatal, ce cancer, n'était traité que par la gastrostomie, associée ou non à la radiothérapie, avec une survie de 6 mois à un an.

Un diagnostic précoce, une préparation préopératoire méticuleuse, une technique basée sur les conceptions actuelles de la chirurgie du

cancer, un anesthésiste de haute compétence, des soins post-opératoires non moins méticuleux, le traitement immédiat des complications post-opératoires éventuelles peuvent abaisser la mortalité de façon notable comme en témoignent les 10 cas opérés par l'auteur, dont 6 publiés antérieurement et 4 cités à la fin du présent travail.

Diagnostic précoce; l'amaigrissement et une gêne à la déglutition chez une personne passée 35 ou 40 ans doivent commander une radiographie et une biopsie. Une alimentation riche en calories, des liquides en abondance, une hygiène buccale sévère, des transfusions, sont essentiels avant l'opération.

Si le cancer est situé dans les deux tiers supérieurs de l'œsophage, on doit pratiquer une gastrostomie préalable. S'il est situé au tiers inférieur, l'œsophagogastrostomie en un temps est indiquée, mais sans pratiquer de pneumothorax avant l'opération. Par contre, l'anesthésie doit être savamment contrôlée en rapport avec la pression pleuro-pulmonaire. Pour le choix de l'opération deux cas à considérer: le cancer situé dans les deux tiers supérieurs et celui du tiers inférieur.

Après extirpation d'un segment supérieur de l'œsophage il est impossible, pour des raisons anatomiques rappelées par l'auteur de suturer avec chance de succès les deux tranches de l'œsophage. Il faut se contenter de l'excision trans-thoracique et de l'extirpation par voie sus-claviculaire suivie plus tard d'un rétablissement du conduit œsophagien extra-thoracique par le truchement d'un tube en caoutchouc introduit en haut à l'extrémité cervicale de l'œsophage sectionné et en bas à la bouche de gastrostomie.

Pour les cancers situés sur le segment œsophagien inférieur (2 ou 3 derniers pouces), et qui font surtout l'objet du présent travail, on doit s'efforcer de réaliser l'anastomose gastro-œsophagienne termino-latérale par voie intra-thoracique et incision du diaphragme.

PIERRE SMITH

Surgical Approach to the Proximal End of the Radius and its Use in Fractures of the Head and Neck of the Radius. Kaplan, E. B.: *J. Bone & Joint Surg.*, 1941, **23**: 86.

The author describes an approach to the head of the radius with careful detail of anatomical structures and their relations, especially to the posterior branch of the radial nerve. The excision extends for about 3 inches, centred at the radio-humeral joint, and in the plane of the lateral intermuscular septum. With the patient prone, the forearm placed in full pronation, the incision deepens between the extensores radialis brevis and longus and the extensor digitorum longus to the orbicular ligament. On section of this ligament, the head of the radius and lateral aspect of the elbow joint are exposed. The radial nerve is safely away from the operation site, being approximately 2 inches below the articular surface of the radius laterally, and 2¾ inches posteriorly, in young patients and relatively more in adults. In the supinated position of the forearm, the nerve is considerably nearer the radial head and neck. Anatomical dissections illustrate the operative approach. This is an excellent surgical approach to the head of the radius which the reviewer has routinely used for some years. H. F. MOSELEY

Obstetrics and Gynæcology

Oral Pregneninolone in the Treatment of Spontaneous Abortion. Krohn, L. and Harris, J. M.: *Am. J. Obst. & Gyn.*, 1941, **41**: 95.

A series of 50 patients with threatened and habitual abortion were treated with oral pregneninolone (anhydro-hydroxy-progesterone) and there were only eight failures. The results obtained with oral pregneninolone compare favourably with and closely approximate those obtained using progesterone in oil. Oral pregneninolone, although not so potent milligram for milligram as progesterone, presents numerous advantages. No undesirable or toxic effects as a result of the administration of this drug were noted. Oral pregneninolone is of distinct value in the treatment of threatened and habitual abortion. ROSS MITCHELL

A Contribution to the Study of Human Fertility. Pryde, J.: *Brit. M. J.*, 1941, **1**: 12.

Data are given from two cases in which the dates of menstruation and of all acts of intercourse were recorded throughout periods of two and three-quarter and five years respectively. In the former case a total of 126 and in the latter case a total of 450 uncontracepted acts were distributed throughout thirty-three and sixty-one consecutive intermenstrual cycles, respectively, at such times that no one of these cycles fell within the tenth to the thirteenth day of the cycles. No pregnancy resulted. On the other hand, when pregnancy was desired it was immediately achieved in both cases following the first uncontracepted acts falling within the tenth to the thirteenth day of the thirty-fourth and sixty-second cycles respectively. These results point to an existence in the cases described of a limited period of fertility within the menstrual cycle, and afford support for the view that such behaviour may be of more general occurrence. ROSS MITCHELL

Ophthalmology

Treatment of Inclusion Conjunctivitis with Sulfanilamide. Thygeson, P.: *Arch. Ophth.*, 1941, **25**: 217.

The virus disease known as "inclusion conjunctivitis", or inclusion blennorrhœa, is an etiological entity which appears in the newborn infant typically as severe papillary conjunctivitis and in the adult as follicular conjunctivitis, with acute or subacute onset. The

disease, whether in the adult or in the newborn infant, heals spontaneously after running a course of at least several months.

In a series of 52 cases observed by Thygeson the conjunctiva had never returned to normal in less than three months, and had required from four to five months in the majority of cases. After the report by Loe that sulfanilamide had proved effective in the treatment of the related virus disease, trachoma, the drug was tested in cases of inclusion conjunctivitis. In Thygeson's series sulfanilamide proved effective in causing rapid healing of inclusion conjunctivitis in infants and adults, as well as of the experimental disease in monkeys and baboons. Adults with predominant papillary hypertrophy responded more rapidly than those with predominant follicular hypertrophy. The characteristic epithelial cell inclusions could always be demonstrated during the first two days of therapy, but could not be found after the third day. Infectivity of epithelial scrappings for baboons also disappeared during treatment. S. HANFORD MCKEE

Subjective "Lightning Flashes". Moore, R. F.: *Am. J. Ophth.*, 1940, **23**: 1255.

The writer previously reported on this symptom-complex, and now furnishes details of 33 additional cases.

The symptom consists of the occurrence of flashes of light, most often likened by the patient to lightning; they are usually vertical in direction, and referred to the temporal side, and are accompanied by the simultaneous development of opacities in the vitreous. They are more common in women. Among the 33 cases, 26 were in women, and this disproportion would seem sufficiently great to indicate a real sex difference. They seldom occur before middle-age, for of the present group 3 patients only were under the age of 50 years, the average being just over 60 years.

The chief importance of the symptom lies in its recognition and the realization that it is not of serious import, nor is it the forerunner of some more serious development. The author feared at first that it might be an indication of vascular disease, retinal detachment, an early neoplasm, or some other malady in the incipient stage. It is a symptom-complex that does not carry any serious implication, either at the time or for the future; it is not a manifestation of migraine. S. HANFORD MCKEE

Neurology and Psychiatry

Psychiatric Casualties in London, September, 1940. Pegge, G.: *Brit. M. J.*, 1940, **2**: 553.

This brief report is intended to show that psychiatric war casualties have occurred, though to a surprisingly small extent so far, probably because a year of war has eliminated by evacuation many neurotic or potentially neurotic people. In discussing the neuroses of war, whether in the armed forces or in the civilian population, there has been much argument as to what cases can truly be said to have been caused by war-stress, and the idea has become prevalent that if a patient has shown the least sign of neurosis in his previous history he cannot rightly be called a war neurotic. The author believes that his clinical material reveals how superficial such an argument is. He points out that there is no absolute dividing line between neurotic and non-neurotic and that probably every one has some trace of neurotic reaction in his adjustment to reality. Therefore, any distinction must be quantitative rather than qualitative. In assessing the war-factor as a precipitating cause of florid neurotic illness it must be decided to what extent any previous neurosis is responsible, jointly with present stress. In this series of 29 cases 9 had a history of pre-existing neurotic illness; 10 had no such history but were said to have been nervous and high strung; 3 showed no discoverable predisposing factors, four showed mild psychotic or psychopathic personalities; 2 were complicated by concussion, and 1 refused examination. Six typical cases are outlined.

The method of treatment is described. Six were treated successfully as out-patients and ten successfully as in-patients in three days. The result of treatment refers only to its effect on the acute incapacitating symptoms.

G. ADAMSON

Dermatology

Experimental and Clinical Observations with Histaminase. Knoll, A. F. and Beinhauer, L. G.: *Arch. Dermatol. & Syph.*, 1940, **42**: 896.

The authors review the history of the discovery by Best and McHenry of a substance in certain organs of the dog, capable of inactivating histamine, and their work and that of later investigators of this substance, called histaminase. They carried out a large number of experiments and clinical trials in animals and man, the series of animals being greater than any previously reported on. Their results appeared to support the view that there is no justification for assuming that histamine is the only harmful cell-constituent liberated by injury, and that consequently one need not expect so specific a substance as histaminase to alter strikingly the anaphylactic reaction. One hundred and thirty-four patients were treated orally with histaminase. Of these 101 suffered from allergic diseases, and 33 from miscellaneous disturbances. Pronounced improvement obtained in only 26.1 per cent of the cases. The unimproved group was treated for six weeks. More than half of the improved group were afflicted with atopic dermatitis or acute urticaria, two diseases which often improve spontaneously. D. E. H. CLEVELAND

Staphylococcic Impetigo Contagiosa. Epstein, S., *Arch. of Dermat. & Syph.*, 1940, **42**: 840.

Epstein shows that while the rôle of the streptococcus in the etiology of impetigo contagiosa has been settled, and the existence of staphylococcic form is still contested by some authors, the latter represents a specific entity with a characteristic clinical picture. The staphylococcic etiology of this type has been established definitely by: (1) the correlation of clinical and bacteriological diagnosis; (2) proof of the etiological rôle of the staphylococcus by special bacteriological methods; (3) the production of typical staphylococcic impetigo by inoculation of *Staph. aureus.* D. E. H. CLEVELAND

Pathology and Experimental Medicine

Cytology of the Gastric Contents, with Special Reference to Gastritis. Mulrooney, R. E. and Eusterman, G. B.: *Arch. Surg.*, 1941, **42**: 55.

Since epithelial desquamation, as well as exudation, is characteristic of mucosal inflammation, it seems reasonable to conclude that cytological examination of the gastric juice under favourable conditions would be of diagnostic value in cases of gastritis. The procedure also promises to be an important adjunct to roentgenoscopical and gastroscopical examinations and to be helpful in determining the effect of treatment of gastritis. The authors assess the results of tests of 50 patients. They offer a technique for study of the cellular elements of the gastric contents after an alcohol test meal which is described in detail. Neutralizing the gastric acids *in vivo* was a definite aid in preserving the integrity of the cytoplasm of the cells of the gastric contents, but the nuclei could normally be differentiated from one another, even though their cytoplasm had been digested away. Results of the test are given of patients with uncomplicated duodenal ulcer, duodenal ulcer with stenosis and secondary gastritis, benign gastric ulcer, gastric carcinoma, persistent gastric symptoms after gastric operations, gastrojejunal ulcer, gastritis. The authors believe that their method of study offers great possibilities for the diagnosis of gastritis and permits a numerical evaluation of the response of the gastric mucosa to therapeutic measures.

G. E. LEARMONTH

Human Sternal Bone Marrow in Hyperthyroid and Myxœdematous States. Jones, R. M.: *Am. J. M. Sc.*, 1940, **200**: 211.

The author found that 12 persons with hyperthyroidism showed an average of 13.5 per cent nucleated cells in the sternal bone marrow, whereas 7 cases of hypothyroidism showed only 2.4 per cent nucleated cells. These findings were compared with 18 control cases in which the average count was 6.2 per cent nucleated cells. In other words, the hyperthyroid cases showed a hyperplastic sternal marrow, and the myxœdematous patients, subnormal marrow activity. Following desiccated thyroid or thyroxin administration the hypothyroid group developed a more normal marrow. After thyroidectomy the marrow of the hyperthyroid cases became less hyperplastic. In all instances the marrow changes were myeloid in character and were not reflected in the peripheral blood. E. S. MILLS

Hygiene and Public Health

Blood Pressure Study, 1939. Compiled and Published by the Actuarial Society of America and the Association of Life Insurance Medical Directors, New York, N.Y., 1940.

The prognostic significance of blood pressure is not universally agreed upon by medical men. Many competent physicians minimize the import of moderate elevations of blood pressure; others magnify it. Insurance carriers have to take things as they find them and without necessarily searching out causes, if significant correlations occur, rates are adjusted to fall in line with them.

A number of studies of blood pressure have been made by insurance actuaries. The latest is the one under review. Essentially the study confirms previous findings that mortality increases as blood pressure increases. Numerous tables are given showing the ratio of actual to expected deaths at different age-groups and at different blood pressures. For the first time the systolic and diastolic blood pressures are considered together. Taking all diseases and all ages together the records show a progressive increase in mortality as systolic blood pressure increases. Those who had systolic blood pressures of under 130 mm. at the time of issuance of the policy had a ratio of actual to expected deaths of approximately 1, while those with blood pressures of 158 mm. and over had a ratio of 2.4. Similar figures are given for diastolic pressures. For entry ages of 40 years and over the systolic pressure appears to be the more important factor and for entry ages below 30 years the influence of the diastolic seems more marked than that of the systolic pressure.

If the analytical procedure is applied to specific diseases it is found, as might be expected, that in the case of the cardio-vascular-renal diseases high mortality was associated with high systolic and diastolic pressures, so too with deaths from cirrhosis of the liver. Deaths from tuberculosis, however, were significantly associated with low blood pressures.

There are 19 tables in the main body of the report and 4 tables in the appendix. A selected bibliography is given. The book is of obvious value to insurance people and should be of considerable interest to the medical profession, particularly to cardiologists and internists.

FRANK G. PEDLEY

Obituaries

David Low, M.D., C.M., F.R.C.S.(C), of Regina, Sask., died on the morning of March 9, 1941, and when the news was passed around there were none who did not experience a sense of loss, although his death was not unexpected. He had been ailing for some time past, and his passing was a release from his distress.

On July 1, 1890, after spending a short time at Prince Albert, Doctor Low came to Regina where he practised medicine and surgery until his death. And as one looked at the oak casket, one felt how, appropriately, it contained a heart of oak that had served the community through the rigorous times of pioneer life from the days of Regina, the village, to Regina, the city, of 60,000; from the days of mud roads and the horse and buggy to the days of pavement and motor cars.

Few of us today know anything of the medical men of this city who preceded Doctor Low, and so look upon him as Regina's first doctor. Time gathered more and more members of the profession around him, with him as their leader and steady guide. In ethical procedure he expressed himself forcefully on many occasions, but always impersonally; his profession was first, he himself last.

The profession of Saskatchewan owes much to him for guidance in the early days during the transition from the North-West Territories to the Province of Saskatchewan and the organization of the Saskatchewan Medical Association of which body he was the president in 1912 and 1913. The profession of Canada will remember him as the president of the Canadian Medical Association in 1926. The Fellows of the Royal College of Physicians and Surgeons of Canada will remember him as the forceful figure of 1927, fighting for the establishment of a Royal College which would be a mark of proficiency for the profession of Canada, distinctively Canadian, and on a par with that of any other country. As the result of this effort the Royal College of Physicians and Surgeons of Canada was brought into being.

Photo by Blank & Stoller Ltd., Montreal

DR. DAVID LOW

His whole life was one of service to the people and profession. No call was too trivial and no obstacle too great to tackle, were it storm, mud, flood, or distance, often at great risk to himself. On occasion it would seem that an unseen hand guided and protected him, otherwise he might have been killed by a train or lost on the prairie.

Doctor Low graduated from McGill University in 1888, and spent two years in internship in Montreal before coming west. He thus was our link with the days of Lord Lister, and he experienced the changing methods of that time. He operated under the carbolic spray and followed all the steps from antiseptic to aseptic surgery. He followed the development of x-ray from the static machine with the revolving disc to the advanced methods of the present. He was a keen student of the microscope and its aid to diagnoses, from its meagre use at the time of his graduation to the advancement of the present day. A keen student throughout.

He came to Regina when there was no hospital and watched the gradual development of our two large institutions, the Regina General and the Grey Nuns. The first accomplishment to that end was only a few rooms in a private home on McIntyre and 11th Avenue in 1889. Later, with the help of some ladies, a better building on 13th Avenue and Hamilton Street was obtained in 1897 which had the first semblance of a hospital. Then through his efforts the Victorian Order of Nurses was induced to open and staff a larger institution on Hamilton and 14th Avenue in 1900, which was taken over by the city in 1907, and thus became the nucleus of the present General Hospital. Dr. Low was a member of the Saskatchewan Cancer Commission from its inception in 1931 until his death.

Doctor Low's opinions were founded on experience and extensive reading. Many of the older men will remember the vigorous arguments he urged in connection with the use of diphtheria antitoxin. He always had the courage of his convictions, and of later years seldom lost the opportunity of jokingly exclaiming, "Why! we did that forty years ago". He was a careful diagnostician, an excellent consultant, and a surgeon of recognized ability. We shall miss his wise counsel and professional bearing in our deliberations of the future.

S. E. MOORE

AN APPRECIATION

With the passing of Dr. Low there has gone from the medical profession of Saskatchewan one of its stalwart, sterling members.

Back in the early days of civilization in Saskatchewan, Dr. Low came to Regina, where his great efforts to relieve pain, cure disease, or mitigate its cause, were always at the call of all, regardless of monetary consideration, exemplifying principles upon which the profession of medicine was built and which have made it what it is. He fought alike the elements of snow, frost, blizzard, mud and slough to carry the benefits of medical science to the unfortunate that they might live. His success in this needs no words of mine. Memory of those deeds of his will live on after him. Not only did he battle against the above most successfully but he battled against the human element outside the profession who sought to sabotage his special calling which he so highly respected and so well represented.

A man of sturdy will and brilliant mind, who, like a mariner on an uncharted sea, laid out his course, made sure he was right, and pursued that course to the end. Such an one is beyond value and to one who knew his great disappointment at the turn of medical affairs when he, physically, was unable to carry the battle to the enemy of his profession, it brought a sting of pain.

Dr. Low was one of Canada's great citizens, as a man, a doctor, a friend, and a patriot and one who fought so hard and honestly for those principles which he knew to be right.

A patriot to his country; a patriot to his profession; a patriot to his conscience.

AN ADMIRER

Dr. John Vassie Brown, of Orillia, Ont., died on April 8, 1941, aged 64. He was born in Barrie, graduated from the University of Toronto (1903) and practised medicine in Orillia for more than 25 years. He served with the Royal Canadian Medical Corps with the rank of captain in the first Great War, having enlisted in 1914 and being discharged in 1918.

Hon. Ernest Choquette, M.D., M.L.C., of Montreal and St. Hilaire, Que., died on March 29, 1941. He was born in Beloeil, Vercheres County, on November 18, 1862, a son of Joseph Choquette and Marie Audet. He attended St. Hyacinthe College, and later went to Laval University Medical School, Montreal, to study medicine. Graduating in 1886 he set up a practice in St. Hilaire. He divided his attention between medicine and literature, and produced some well-known French-Canadian works, including "Claude Payson," "Les Ribaud," "La Terre" and "Carabinades," works of which outstanding critics wrote appreciatively.

His third interest was politics, which finally superseded medicine in the first place among his public activities. At a comparatively early age he abandoned medical practice to devote himself to politics and literature, and in both of these fields he became an outstanding figure.

His long and successful services to the province as a Liberal campaigner at many elections and also as a frank and fearless counsellor and critic from within the Liberal party earned him his nomination in 1910 to the Upper House in Quebec, where he succeeded the late Hon. F. Gosselin as member for Rougemont.

Dr. Choquette was a member of the Royal Society of Canada as well as a Governor of Quebec's College of Physicians and Surgeons. He belonged to the Reform Club, the Club Canadien, and the Canadian Authors' Association. For many years he was mayor of the parish of St. Hilaire.

The death of **Dr. T. H. Eastwood** was recorded last month in the *Journal*. The following "Appreciation" by Dr. G. Stewart Cameron, of Peterborough, was sent us too late for earlier publication.

AN APPRECIATION

John Havelock Eastwood died in Peterborough on February 17, 1941. Born at Pickering, Ontario County, in 1866, he was one of the older physicians of this city. Notwithstanding this seniority, he continued in the active practice of his profession until a short time before his death. His father before him was a doctor—one of that splendid body of country practitioners who assisted in laying the foundations of medical practice in this Province. The son was proud of this heritage, and sought at all times to maintain those traditions of the healing art with which he had been surrounded in early life.

After the usual pre-medical education of the day, Doctor Eastwood entered the Faculty of Medicine of the University of Toronto, from which he graduated in 1887. After some six years of practice in Pickering he moved to Peterborough, where he early secured and maintained the confidence of a large circle of patients and friends. He engaged in general practice until 1920, when he joined with other medical associates in forming the Standard Medical and Surgical Clinic. From this time on he devoted most of his energies to pædiatrics, in which department he established more than a local reputation.

Of a retiring disposition, Dr. Eastwood did not seek the more exhilarating field of medical politics. This reticence, however, did not indicate any lack of interest in the general welfare of his profession. On the contrary, he believed the practice of medicine to be a great influence for the betterment of human lives, in as much as good citizenship is more likely to be built on a foundation of sound minds in sound bodies, nurtured in healthful suroundings.

He was keenly interested in the intelligent development of his country and his own community, and always supported those who, in his estimation, were most likely to give selfless leadership, regardless of their political or religious affiliations. In his earlier years he was fond of cricket and curling, but later golf claimed him as a faithful disciple.

His wife, who survives him, was Miss Paxton, of Whitby. Two sons, William of Peterborough and Hubert of Hamilton, and one daughter, Mrs. Alex. Donnelly of Peterborough, are left to mourn the loss of a devoted father.

The funeral service in Saint Andrew's Church was very largely attended and was a striking evidence of the esteem in which he was held. Into many a troubled home he came and seldom did he depart without leaving behind some encouragement, some word or act that sought to ease the burden resting upon those to whom he had come to minister either as physician or as friend.

Dr. Howard Roxboro Elliot, of Grimsby, Ont., died on April, 1941, in his eighty-third year. Dr. Elliot was born in Iroquois, Ont., and practised for 58 years. He graduated in medicine from Victoria College, University of Toronto, in 1881 and in the following year took his L.R.C.P., L.R.C.S. in Edinburgh. Returning to Canada, he started his career at Brucefield, Huron County. After eighteen years in Huron County, Dr. Elliot moved to Denver, Col., where he practised for forty years. Five months ago he came to Grimsby to retire.

Dr. Alexander Jardine Hunter, of Teulon, Man., died on August 25, 1940. He was born in 1868 and a graduate of the University of Toronto (1895).

Dr. John Lachlan MacIsaac, of Antigonish, N.S., died on March 24, 1941.

Dr. MacIsaac was born at Dunmore, Antigonish county, on June 3, 1870, and was the son of the late Lachlan and Mary (MacIsaac) MacIsaac. After attending the schools at Dunmore and St. Joseph's he studied at St. Francis Xavier, breaking his course to teach school. In 1898 he went to British Columbia where he worked until 1903 as a lineman. He graduated from the Baltimore Medical College in 1907, came back to his native county and started his practice in Antigonish. He had been there ever since, and nearly every year had taken post-graduate courses at hospitals in Montreal, New York, Baltimore, Chicago and at the Mayo Clinic at Rochester, Minn.

In 1920 he was elected a Fellow of the American College of Physicians. In 1925 he was elected to represent Antigonish county in the Provincial Legislature and had been re-elected at every election since. He was a valuable member, and his studied opinion has been of great value to his province. About ten years ago he was a member of a commission appointed by the Provincial government to look into the flour mill situation. From 1925 to 1928 Dr. MacIsaac was one of an opposition of three, the others being the late Hon. William Chisholm, of Antigonish, and D. B. MacLeod, Victoria county. He always took a great interest in St. Martha's Hospital, from its humble beginning to the large institution it is now. His fame as a surgeon went far beyond the province.

Dr. William Robertson, of Elora, Ont., died on March 30, 1941, at the age of seventy-six. A native of Chesterfield in Oxford County, he was a son of the late Rev. William Robertson, and a grandson of the late Rev. William Duff, former minister of Knox Presbyterian Church in Elora. He was a graduate of McGill University (1890) and had been Medical Officer of Health for Pilkington Township for many years. He had practised in Elora for fifty-one years.

Dr. Hugh McLean Scott, of Morriston, Ont., died in February, 1941, in his thirty-sixth year. Born at Badenoch, in Puslinch Township, a son of Mr. and Mrs. Andrew Scott, Dr. Scott received his secondary education at the Guelph Collegiate and later graduated in medicine from Queen's University (1929). After serving a year as intern at Victoria Hospital, London, Dr. Scott opened

a practice at Lucan, which he conducted for four years before coming to Morriston.

Dr. William Woodhouse Scott, Hazelridge, Man., died on March 19, 1941, in his seventy-ninth year. A son of the late Rev. John Scott, pioneer missionary of Emerson, Dr. Scott was born in Napanee, Ont., and came to Emerson with his parents in 1876. He graduated from Manitoba Medical College in 1895 and from then until 1916 practised medicine in Walhalla, and for the last 20 years in the municipality of Springfield, Man.

Dr. Manley Adair Shipley, of Kirkland Lake, Ont., died on April 8, 1941, aged forty-four years. He was a graduate of the University of Toronto (1925).

Dr. Arthur Alexander Johnston Simpson, of Kintail, Ont., died on March 21, 1941, in his seventy-eighth year. The late Dr. Simpson was born near Walkerton, son of the late Arthur Simpson and Margaret Johnston Simpson, early pioneers of that district, both of whom came from Aberdeen, Scotland. He received his elementary school education in the rural school, afterwards going to High School in Walkerton and Owen Sound, where he also attended Model School. After teaching in Culross for two years, he attended Normal School in Ottawa, and, following in the footsteps of his father, who was a school teacher, he taught for seven years at Britannia Bay, near Ottawa. He was a graduate of Trinity University, Toronto (1904). After interning at Singhampton with Dr. Ball, he was assistant for a short time to Dr. Elliott of Lucknow, and then went to Kintail, where he established a flourishing rural practice which he continued for thirty-seven years, until his death.

Dr. Roland Earl Taylor, of Windsor, Ont., died on March 14, 1941. Dr. Taylor was forty-four years of age, was born in Woodstock and educated in Woodstock public and high school. He graduated from the University of Toronto in 1922. For a short time he practised in Burgessville and came to Windsor in 1924.

While still a student Dr. Taylor enlisted during the First World War and served in France for two years as a signaller with the Canadian Expeditionary Force.

He was an honorary member of the Canadian Legion branch at "The Hut"—Ward Two.

Dr. Taylor belonged to the staff of Windsor's three major hospitals, Grace, Metropolitan General, and Hotel-Dieu.

His deep concern was the well-being of humanity and his unselfish devotion to the profession which he honoured, was a tradition among those associated with him. His inspiring service and untiring devotion to those whom he served will ever remain with us. J. A. LEO WALKER

News Items

Alberta

The annual refresher course arranged by the Canadian Medical Association, Alberta Division, and the University of Alberta, arranged for the week commencing May 12th, was held in the University Hospital, Edmonton. In order that the course should cover the points desired by the prospective registrants, a plebicite was taken of the profession in Alberta, which was well responded to. In addition to the medical staff of the University, the following clinicians were present: Dr. J. D. Adamson, Winnipeg; Dr. Charles B. Puestow, Chicago; Dr. E. P. Scarlett, Calgary. Dr. Adamson is professor of medicine in the Manitoba University and Dr. Puestow is second in command of the educational research hospital in Chicago.

Arrangements have been made for five district meetings to be held the first week in June, commencing at Red Deer on June 2nd and continuing for five days. They will cover Calgary, Lethbridge, Medicine Hat and Drumheller as well as Red Deer. The following will make the tour: Dr. J. Ross Vant, Edmonton, President-elect, Canadian Medical Association, Alberta Division; Dr. R. B. Francis, Calgary, President, College of Physicians and Surgeons; Dr. J. K. Fife, Edmonton, Surgeon; Dr. James Calder, Edmonton, Pædiatrician; Dr. George R. Johnson, Calgary, Registrar, College of Physicians and Surgeons.

In addition to addressing the meetings as President-elect, Dr. J. Ross Vant will give a scientific paper on obstetrics at each meeting. As these are annual meetings the elections for officers for the coming year will take place.

The Department of Health has developed a system of district nursing to the point where they now have 33 well trained and efficient women rendering nursing service in the outlying and sparsely settled districts. While people who are able to pay are supposed to contribute a nominal fee, in actual practice, the service is rendered gratis for the most part.

The Committee of the Division dealing with co-operation with the Department of Militia in recommending suitable medical men for various posts, has been quite active and is meeting with the D.M.O. early in April to further assist the department.

Recently there was laid on the table of the Legislature, the annual report, which for the first time analyzed the expenses of the medical-aid fund. For some time the workmen, in reading the report, have considered money from this fund was going to the medical men in its entirety, which has created a false impression, and some unions have felt that the doctors' fees must have been too large. It was openly stated by people without knowledge that the physicians received more monev from the Board than the workmen did from the Accident Fund, which was quite wrong, as the following figures show:

Payments from Pension Fund to permanently disabled workmen, and dependents of those fatally injured ...	$443,487.34
Payments of compensation and other allowances to workmen	402,322.01
Other benefits and services to injured workmen	15,497.49
	$861,306.84
Payments to attending physicians and specialists	$127,521.85
Hospitalization and other services	194,586.35

By the above it will be seen that while the workmen received $861,000 of which $402,000 was for compensation, the physicians caring for them received only $127,500. It is felt that all future reports should thus divide the Medical Aid Fund to show the actual payments to members of the profession. The Board reports that the average accident case is costing less and less as time goes on, and that from physical therapy they are getting marked beneficial results.

The Department of Health has opened its diagnostic and treatment clinic in Calgary, with the following as members of the staff: Drs. J. W. Richardson, surgeon; R. R. Hughes, physician; W. S. Quint, radiologist; R. C. Riley, pathologist.

It is understood that the cases are to be diagnosed at the Holy Cross Hospital and patients likely to be cured or benefited by deep x-rays or radium therapy will be referred to Dr. W. H. McGuffin at the Radium and X-ray Institute. G. E. LEARMONTH

British Columbia

The following men were elected to the Council of the College of Physicians and Surgeons of British Columbia: District No. 1, Drs. F. M. Bryant and Thomas McPherson; District No. 2, Dr. W. A. Clarke; District No. 3, Drs. H. H. Milburn and Wallace Wilson; District No. 4, Dr. Osborne Morris; District No. 5, Dr. F. M. Auld. Of these the following are newcomers, Drs. Auld, Bryant, Milburn and Wilson.

The vital statistics for British Columbia, and especially Vancouver, are gradually attaining a very high standard of excellence. Dr. Stewart Murray, M.H.O. for Vancouver, states that the infant mortality for Vancouver during 1940 was the lowest of any large city in the world, while maternal mortality has also reached a record low figure for North America. There was not a single case of diphtheria during 1940. These facts reflect considerable credit on the work of the Public Health Department of British Columbia and upon hospital conditions in this province.

The British Columbia Cancer Institute reports some interesting and important facts. Fifty per cent of those attending come from points outside Vancouver where the Institute is situated. The greatest need of the Institute is hospital facilities for those requiring hospitalization, although the Vancouver General Hospital, which is always over-taxed as regards bed capacity, has co-operated most loyally and given every aid possible. The public sympathy and support for the work of the Institute is growing, and a movement is on foot to attack this problem aggressively and increase facilities for the work of the Institute.

Dr. G. F. Amyot, Provincial Health Officer, speaking at a recent meeting, made a strong appeal for better reporting of cases of cancer. As things are at present this is practically non-existent, except on the death certificate of those dying of cancer.

A very well-attended meeting was held on April 1st in the Auditorium of the Medical Dental Building in Vancouver when the Committee on the Study of Cancer of the British Columbia Medical Association put on a program dealing with all aspects of cancer—diagnosis, symptomatology and therapeutics. Men from all parts of the province attended, and papers were contributed from Victoria. J. H. MACDERMOT

Manitoba

At the request of the Manitoba Medical Association the Department of Health and Public Welfare instituted an inquiry into the causation of prenatal, natal and neonatal deaths occurring in Manitoba.

Figures for the first six months from May to October, 1940, inclusive, have been released. For this period there were recorded 6,277 live births, 161 stillbirths, and 153 deaths of children under 14 days of age. This gives a death rate for children between 28 weeks' gestation and 14 days of extrauterine life of 48.6 per 1,000 births. Of every 100 children who have reached 28 weeks of life within the womb almost 5 die within the next three months. The mortality rate of Indian children is nearly four times that of white children: Indians, 183, whites, 46 deaths per 1,000 live births.

Two hundred and seventy questionnaires have been sent out to doctors certifying stillbirths and deaths of children under 14 days of age for the period under review, and of these returns have been made of 214, or 79 per cent. As no payment is made for filling out these questionnaires a return of nearly four out of every five must be considered a high figure.

Of the 214 deaths 54 have been due to complications of labour; 32 to diseases of the mother; 37 to anomalies of the placenta, cord and membranes; 33 to abnormal development of the fetus; and only 14 to diseases which might be termed post natal. In this series of 214 deaths the forceps deliveries numbered 22 per cent and Cæsarean sections, 1.5 per cent.

A study of the returns in connection with the 214 deaths indicates that risk to offspring increased with a rise in the age of the mother and in the later pregnancies.

A survey of health activities in Manitoba will be made by the American Public Health Association, beginning about May 1st. Hon. J. O. McLenaghen, K.C., Minister of Health and Public Welfare has announced that his department will co-operate in the survey. City and suburban health departments and the Winnipeg School Board have also agreed to help.

The survey will be made by staff experts and at the expense of the American organization. Its object will be to determine if the best possible health facilities are being provided, and if the activities of the provincial health department are of greatest possible service in the war effort.

A 25-bed medical building will be erected shortly at Stevenson Field, Winnipeg, to provide extended facilities for Royal Canadian Air Force units. The building, which will probably be placed on the premises of No. 8 Repair Depot, will be the standard air-force type, similar to the medical building at the Tuxedo wireless school. It will contain facilities for providing short periods of treatment for air-force personnel. Airmen who require extended hospitalization are sent to Deer Lodge or other hospitals, approved by the Department of Pensions and National Health.

The Senate of the University of Manitoba adopted the recommendation from the Medical Faculty Council Executive, and approval has been given to a plan for the conduct of the final year examinations in medicine co-incidentally with the examinations of the Medical Council of Canada. This action has been received with great satisfaction both by medical students and members of the Medical Faculty.

A renewal contract has been signed by representatives of the medical profession in Winnipeg and the Firefighters' Club to provide a complete medical service for the year commencing April 15, 1941. The dues collected from the members of the club will be on a considerably higher scale, as the first year's experiment showed that much more service was required than had been anticipated. About one person in twenty received major surgical treatment.

The Firefighters' Club has expressed its satisfaction with the medical services rendered by the profession during the past year. ROSS MITCHELL

New Brunswick

Dr. E. A. Petrie, Radiologist at St. Joseph's Hospital, Saint John, has been elected a member of the American College of Radiology.

Dr. N. Skinner was the speaker at the monthly meeting of the Saint John Medical Society held in the Admiral Beatty Hotel on March 25, 1941. Dr. Skinner reviewed a number of case histories from his own practice in which allergy was the deciding factor in diagnosis. Dr. Skinner has been especially interested in this particular branch of medicine for some time and his presentation was much appreciated by the large number in attendance.

Dr. S. R. D. Hewitt, Superintendent of the Saint John General Hospital, has been a patient in his own institution for some weeks. He has now returned home for convalescence.

Dr. Hugh Farris, of Saint John, has returned home from a holiday spent at Nassau.

In spite of difficulties with foreign exchange, a number of local physicians are contemplating post-graduate courses in the United States. Dr. N. Skinner is leaving next week for a refresher course in gastro-enterology, in Boston.

Dr. R. A. H. Mackeen, Provincial Pathologist, has been appointed Hospital Pathologist at Camp Sussex. Dr. Mackeen was a lieutenant in the R.C.A.M.C.(R.F.) and has now been transferred to the active force.

For some time the local press of New Brunswick has contained references to the employment of an unregistered physician in the Provincial Hospital for the Insane at Saint John. The impression has been fostered by certain individuals that the physicians in New Brunswick, through their Council of Physicians and Surgeons, have been persecuting this physician who happens to be a European driven from his home due to wartime conditions. The Registrar of the Council, Dr. J. M. Barry, made it very clear last week in a letter printed in the local newspapers that the physicians in New Brunswick were only interested in that fact that this man was employed by the Provincial Government in a position of responsibility without proper registration. The refugee physician in question had twice tried the Dominion Medical Council examinations in Montreal and had twice failed. The physicians in New Brunswick were only asking that this refugee physician follow the same rules and satisfy the same qualifications as the young physician, born, bred and educated in Canada is forced to satisfy.

A. S. KIRKLAND

Nova Scotia

"Viewed as a whole, the state of the public health (in Nova Scotia) is encouraging, and the favourable trend in those diseases which are amenable to the intervention of physicians and health officers continues." Thus was summed up the health of the province, as tabled in the legislature by the Department of Public Health. Examination of mortality tables for 1940 showed a decrease in communicable diseases with the exception of whooping-cough and tuberculosis. While tuberculosis deaths jumped by 12 to 428, the figure was not out of keeping with the record low of the past two years. In typhoid, measles, scarlet fever, diphtheria and syphilis, the mortality rate showed a new minimum.

"The advent of war has thrown extra burdens upon all important personnel of the department," the report states, adding that close co-operation with the national defence authorities has been maintained.

Fatalities were: heart disease, 997; cancer, 730; tuberculosis, 428; whooping-cough, 60; venereal diseases, 33; diphtheria, 15; scarlet fever, 3; measles, 3; infantile paralysis, 3; typhoid, 2; infant mortality, 64; maternal mortality, 49.

Dr. C. H. Best addressed a public meeting at Halifax to arouse interest in the development of a blood donor scheme to provide reserves of dried serum. A resolution pledging support to the project was passed unanimously.

Testing of more than 100,000 heads of cattle for tuberculosis, in six counties, revealed 0.4 per cent reacting.

The usually circumspect *New York Times* outraged Halifax with a too vivid account of its infectious disease problem, describing the crowded port, in the words of its informer, as a "hell-hole of infection". The informer was one of the group of Harvard bacteriologists and technicians who had come to Halifax to study contagion with a view to solving United States army problems. The Boston reporter, besides interviewing the informer, had studied the official report of Dr. J. H. Mueller, head of the group. He told of the bacteriologists, an heroic band, braving death as their plane dipped into the Halifax germ-laiden air, bringing succour—keeping the port open to send its convoys to Britain, to win the war. Their epic he pictured as a new, stirring chapter in modern medical history.

Halifax officials and citizens who had greeted the visitors warmly, and with happy memories of the Massachusetts aid after the Halifax explosion of 1917, felt bad. So did Dr. Mueller. He flew back immediately to make apologies and public reparations. The new history chapter closed on a restrained note.

Colchester County Hospital at Truro, after discussing, at its meeting, the busiest period it has known, decided that further space was essential, and began arrangements to take over a part of the Maritime Home for Girls as a maternity hospital.

The Halifax Municipal Council has recommended to the Department of Health that it consider giving a bonus to doctors willing to undertake rural practice in communities now without medical aid. This would take the form of a guaranteed minimum income.

ARTHUR L. MURPHY

Ontario

The Hamilton Academy of Medicine and McMaster University have combined, for the seventh consecutive year, to bring to the science students of the University and to the physicians of District Number Four, Ontario Medical Association, a series of scientific lectures dealing with the newer advances and the treatment of disease. This year's lectures have covered the field of radiation therapy. The first lecture dealt with fundamentals of x-ray, radium, ultra-violet, short wave and like radiation; a second dealt with the practical application of the various methods of radiation therapy.

It has been pointed out that the mortality rate of cancer in Ontario doubled during the period 1919-1938. In 1938, 12 per cent of all deaths in the province were due to cancer, a rate of 120 per 100,000. The rate for Hamilton was 106 and for Toronto, 130.

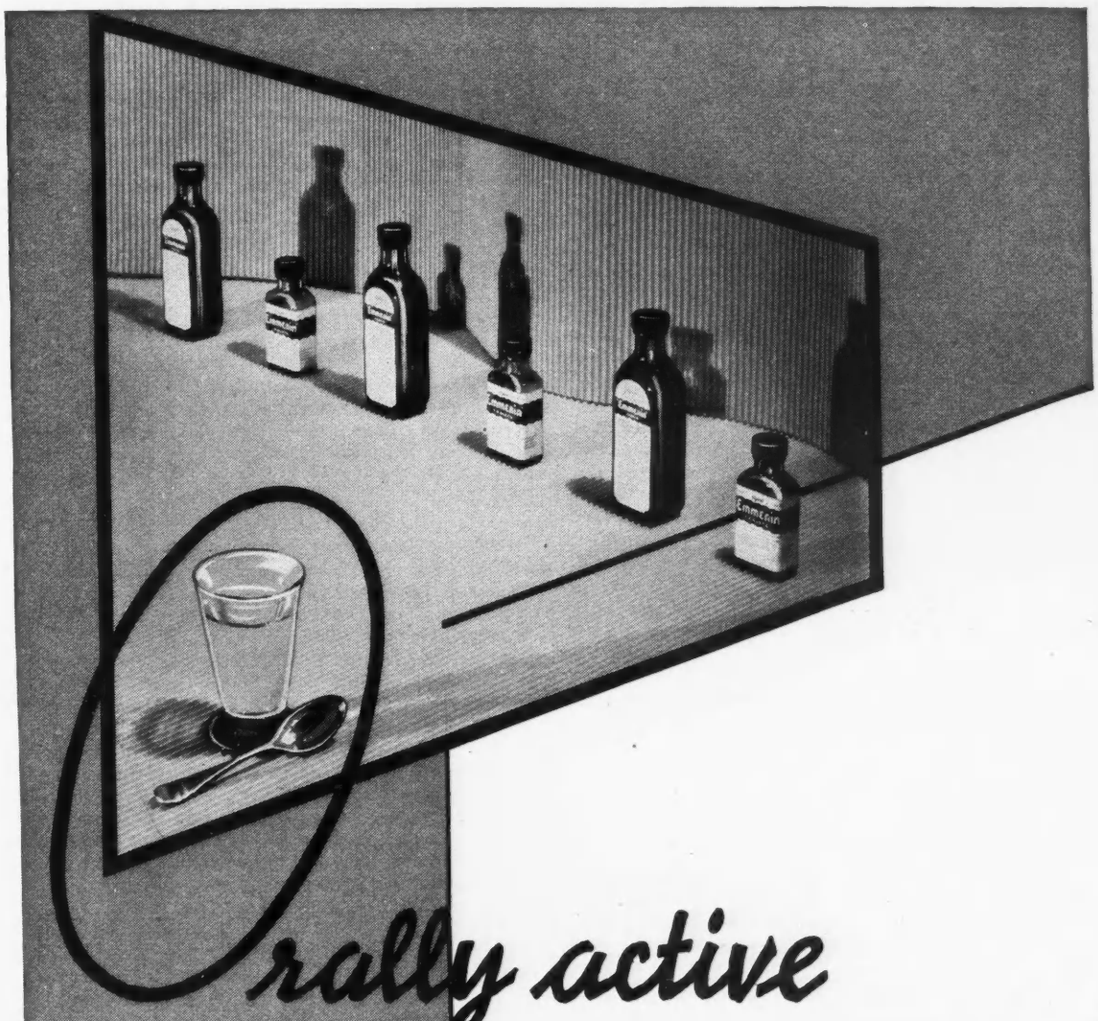
The Education Committee of the Ontario Medical Association for District Number 1 announces a course of post-graduate studies in Military Medicine, Fracture Therapy, Traumatic Surgery, and Cancer Diagnosis, at the University of Western Ontario, London, each Wednesday from April 23rd to May 21st, inclusive. A second part of the annual post-graduate course will follow in September and October.

Dr. M. H. V. Cameron, of Toronto, has been re-elected President of the College of Physicians and Surgeons of Ontario.

Dr. William McClure, who was a student in medicine under Osler at McGill University, and has had a brilliant career in Honan since 1888, has reached his eighty-fifth birthday. On this day he was at home to a number of his friends. A letter of over fifty years ago, written by the Secretary of the Foreign Missions Board, recorded how Osler had considered Dr. McClure one of his best students, and feared that he would be wasting his life in China.

Dr. P. H. Huyck, of Kingston, delivered his maiden address as President of the Ontario Motor League on March 11th, driving from Toronto to the Falls through the blizzard that raged that morning. Active in the past as President of the Kingston and Frontenac Medical Society, he should be a source of great strength to the Motor League.

The Section on Historical Medicine of the Academy of Medicine, London, marked Lister Day by a special program at the Victoria Hospital. Dr. G. A. Ramsay dealt with the historical development of wound healing, followed by Dr. S. A. MacDonald, A. J. Grace,



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and R. A. Johnston, dealing with wound healing and drainage. The luncheon address was given by Dr. G. W. Stavraky, "Lister as a physiologist".

Lister Day at the University of Toronto was marked by the annual address founded by Dr. Donald C. Balfour, of the Mayo Foundation. The guest speaker on this occasion was David Cheever, A.B., M.D.(Harvard), F.A.C.S., Associate Professor of Surgery Emeritus, Medical School of Harvard University, who spoke on the subject, "War: its toll and its tributes".

Plans are under way for the official opening of the three newly completed hospitalization and active treatment units at Westminster Hospital, London. The cost of construction program and equipment has been approximately $400,000.

The Ontario Hospital Association is offering to the public a Plan for Hospital Care. The Board of Administration is to serve without pay. The benefits afforded subscribers are, twenty-one days of hospital care each year, with standard or semi-private accommodation, including meals, dietary, and general nursing service, and the use of the operating room as often as necessary, together with anæsthesia, ordinary drugs and medication, dressings and laboratory service. For maternity care, one-half hospital charges up to twelve days. There is no age limit. The monthly rates are 50c. and 75c. for the individual subscriber; $1.00 to $1.50 for the family. The higher rate provides semi-private accommodation. J. H. ELLIOTT

Quebec

L'Organisation panaméricaine de la lutte contre le cancer tiendra un congrès en 1942 à Buenos-Ayres, Argentine. Le Dr. Ernest Gendreau, membre du Conseil d'administration de cette organisation, vient de se voir confier la direction de cette lutte au Canada.

On annonce les quatre nominations suivantes à l'hôpital Ste-Justine: le Dr Gaston Lapierre qui devient F.R.C.P. (Canada); le Dr Edmond Dubé, F.R.C.S. (Canada); le Dr N. R. Bouziane, Fellow du Canadian Institute of Chemistry, et le Dr Maurice Bonnier, Fellow de l'American College of Chest Physicians.

Le rapport du Service de Santé pour 1939 nous apprend que 13 enfants d'âge scolaire sont morts de diphtérie. Ces enfants n'avaient pas été immunisés. Ces morts inutiles sont imputables à la négligence. La campagne de prophylaxie doit continuer pour éteindre définitivement cette maladie évitable.

Pour la quatrième fois depuis 1928 le bill des chiropracticiens a été battu le 19 février dernier au comité des bills publics de l'Assemblée Legislative par 10 voix contre 7.

Deux hôpitaux annoncent des cours de perfectionnement en pédiatrie: l'hôpital Ste-Justine et l'hôpital de la Miséricorde. An premier hôpital les séances auront lieu du 2 au 7 juin et seront dirigées par le Dr Gaston Lapierre. Au second hôpital elles auront lieu du 7 au 12 juillet et la direction en a été confiée au Dr Paul Letondal.

Le Dr D. Léonard vient d'être chef du service d'électro-radiologie de l'hôpital Notre-Dame. Le Dr Georges Hébert, du même hôpital, a été nommé secrétaire français de la Canadian Medical Association, division de Québec.

La Société Médicale de Montréal a consacré sa séance du 18 mars dernier aux hémorrhagies méningées médicales, obstétricales et chirurgicales. Les rapporteurs ont été, dans le même ordre, les Drs. Antonio Barbeau, Donatien Marion et Albert Guilbeault, Jean Panet-Raymond.

Pre-employment Medical Examinations for Domestic Workers in Montreal.—At a recent meeting of the Section of Pædiatrics of the Montreal Medico-Chirurgical Society, the question was discussed of the risks of contact infection, especially to children, in the home, and the advisability of medical examinations for domestic employees. A committee was accordingly appointed under the chairmanship of Dr. Aubrey Geddes to explore ways and means of providing a centre for the examination and health certification of household workers, and to conduct a campaign of educational publicity.

The American Academy of Pædiatrics has been interested in this question of contact infection for some time, and systems of examination have been introduced in several cities. Arrangements are going forward satisfactorily, and it is hoped that adequate facilities will soon be available in Montreal. JEAN SAUCIER

Saskatchewan

With infant mortality rate the lowest yet recorded, the birth rate the highest in five years, and low general and maternal mortality rates, Regina had an excellent health record in 1940, according to Dr. G. R. Walton, city medical health officer.

During the year 39 infants under one year died, a mortality rate of 39.4 per 1,000, compared with 45.6 the previous year and 59.4 in 1937. Only one mother died in childbirth compared with 6 in 1937. Deaths from all causes totalled 345, yielding a rate of 6.4 per 1,000 compared with 6.1 in 1939 and 6.5 in 1937.

With a death roll of 140, diseases of the heart, arteries and kidneys took highest toll of Regina residents in 1940, nearly one-third of the total. Cancer, with 45 deaths, compared with 56 the previous year, maintains its reputation as a killer. Pneumonia caused 29 deaths and there were 21 accidental and violent deaths in the city. Tuberculosis accounted for three deaths, the lowest in several years.

From a public health viewpoint the most serious event of the year was the occurrence of 11 cases of diphtheria, of which 4 were fatal. In the previous five years only 11 cases and 2 deaths occurred, though Regina's expected incidence from this disease is 153 cases annually. As a result of an educational campaign 2,080 children, of whom 744 were under school age, were inoculated against diphtheria by the department last year and many more were similarly treated by private physicians.

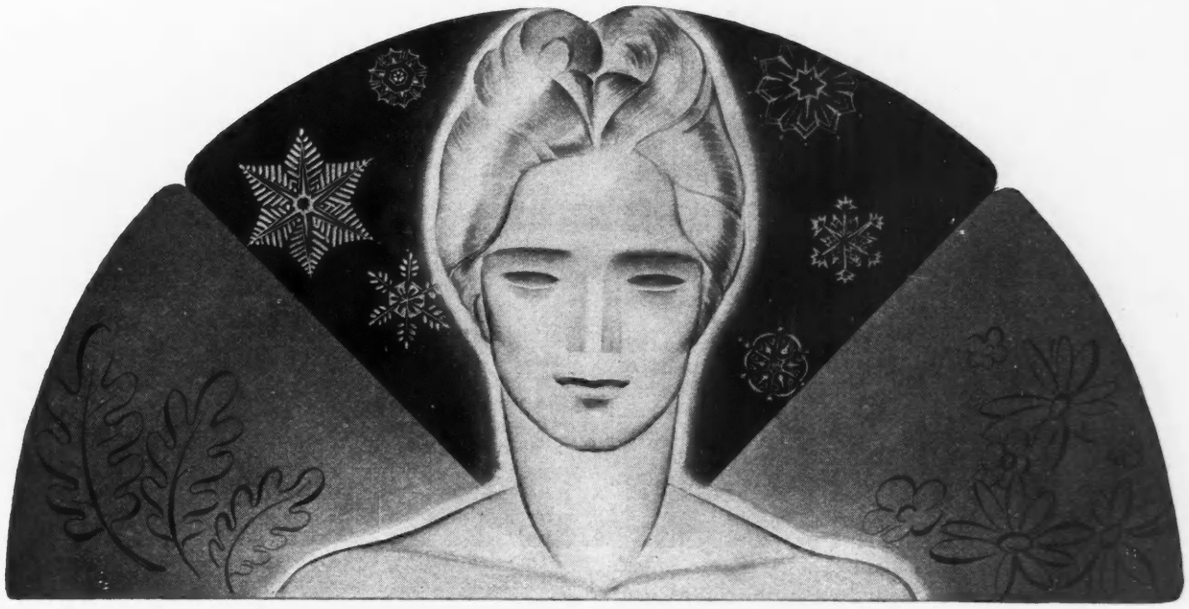
Fewer cases of scarlet fever were reported than in any year since 1915, some 5,000 children having been inoculated against this disease since 1937. There were 2,531 cases of measles, a disease against which there appears to be no means of protection. Chicken-pox accounted for 415 cases.

In the total of 3,770 cases of communicable diseases of all types in 1940, Dr. Walton does not include 501 cases of German measles reported in the last four months of the year, as "I am certain that cases of this disease were poorly reported, many occurring that we never heard of. This is explained by the fact that the disease is an extremely mild one, frequently causing no symptoms except a rash that soon disappears."

There was no smallpox in 1940. Only 29 new cases of pulmonary tuberculosis were discovered at the clinic, and but 4 cases of typhoid fever were reported.

"Tuberculosis," said Dr. Walton, "can and is being controlled. Typhoid, smallpox and diphtheria can be prevented, and much can be done to control other diseases. The prevention and control of communicable disease is of even more importance during war than at other times."

At the annual meeting of Medical Services, Incorporated, Regina, it was reported that 234 subscriptions had been paid up. The following surgical operations were performed during the year for subscribers: one sub-



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mucous resection, one hysterectomy and appendectomy, four tonsillectomies, one appendectomy, one blood transfusion, and four fractures were set.

Dr. R. McAllister, of Regina, has been appointed by the Minister of Health to the Cancer Commission to take the place of the late Dr. David Low.

The regular meeting of the Regina and District Medical Society was held on Friday, March 21st. Dr. Lorne H. McConnell, neurosurgeon of Saskatoon, spoke on "An analysis of 91 craniotomies in the treatment of epilepsy". His talk was illustrated by slides.

In answer to Dr. E. A. McCusker's request from the First Division for medical journals, the Regina and District Medical Society have sent the following journals to the First Division: *Canadian Public Health Journal, Canadian Medical Association Journal, War Medicine, Journal of Surgery,* also the *Year Book in Surgery.*

LILLIAN A. CHASE

General

The Thirteenth Annual Congress of the Canadian Public Health Association will be held in the City of Quebec on June 9th, 10th and 11th. The President this year is Dr. Jean Gregoire, Deputy Minister of Health, Ministry of Health, Quebec.

Book Reviews

Practical Handbook of the Pathology of the Skin. J. M. H. Macleod and I. Muende. 2nd ed., 415 pp., illust. 42s. net. H. K. Lewis, London, 1940.

This is an excellent handbook, not too long, and, at the same time, as its title indicates, practical. McLeod's work first appeared in 1903, and it is curious that his subject has attracted little or no attention until now. His book has been out of print for years; we are pleased to see his teaching brought forward again.

This book is simply and logically planned, but there is no bibliography. The descriptions throughout are excellent, especially that dealing with the minute structure of the corium and other components of the normal skin. The chapters on bacteria and dermatophytes are particularly good. The general pathologist will be impressed with the detailed instructions given for the staining of the skin. In each chapter, also, can be found methods for dealing with its special structures. The work is well illustrated with good drawings, photographs and coloured pictures.

"McLeod and Muende" stands in the front rank of "Histologies" and cannot be too highly commended.

Man's Greatest Victory Over Tuberculosis. J. A. Myers. 419 pp. $5.00. C. C. Thomas, Sprinfield, 1940.

This is an interesting account of the men and the means responsible for the marked reduction in the incidence of tuberculosis in dairy cattle throughout the world in recent years, and the virtual eradication of bovine tuberculosis in the United States of America in the past two decades. The author gives much of the credit for this great victory over tuberculosis to veterinarians who have had the vision and the courage to translate well established facts regarding tuberculosis into action. After describing the place of the tuberculin test in the detection of tuberculosis in cattle and the effectiveness of slaughter of infected animals in the control of tuberculosis in cattle, he points out that in man chest roentgenograms of persons giving a positive intradermal tuberculin test afford a ready and reasonably accurate means for the detection of tuberculous lesions and that segregation of contagious cases of tuberculosis is, from the standpoint of the health of the community, an effective means for the control of tuberculosis. He concludes that physicians who are interested in the control of tuberculosis in human subjects can learn many lessons from veterinarians.

Observations Made During the Epidemic of Measles on the Färoe Islands in the Year 1846. P. L. Panum. 111 pp. $2.50. Am. Public Health Association, New York, 1940.

This small volume is a translation from the Danish of the observations made by Doctor Peter Ludwig Panum during an epidemic of measles on the Färoe Islands in 1846. It not only gives a fascinating description of the islands and their inhabitants, but relates as well how this recent graduate from the University of Copenhagen was selected by the University to proceed there for the purpose of combating a particularly violent epidemic of measles. His energy, initiative, and ability under conditions which offered the very best opportunities for investigation resulted in the recording of his "Observations" which have become a classic in medical literature.

One has but to consider the progress that has been made in medical science during the last fifty years to understand the difficulties that confronted investigators one hundred years ago. Without the aid of laboratories, without a great volume of established medical data, and without the instruments of precision such as we have today, this young physician by the powers of observation and assembling of results gave to medical science the life-history of measles. He established beyond doubt the infectious character of the disease and determined its period of incubation.

It was commonly believed in his day that measles might arise spontaneously, that the incubation period might be even less than ten days, and that the time of desquamation was the time of greatest danger from infection. Not knowing how the disease was carried he stressed isolation, and determined that fourteen days was the incubation period following contact with a previous case in the stage of eruption.

The life-history of this remarkable physician reveals a continual fight against conditions that would have discouraged any but a man of high ideals, abundant energy, and great perseverance. These combined with great tact and personal charm enabled him to exert a powerful influence in his later years on the development of modern physiology and medicine.

Every student of medicine should read this book, to learn how the "humdrum" of everyday practice may be turned into a stimulating adventure.

Treatise on Medicolegal Ophthalmology. A. C. Snell. 312 pp., illust. $7.00. McAinsh, Toronto, 1940.

The author is known widely for his numerous and fundamentally important papers on the medicolegal aspects of ophthalmology. It is not surprising, then, that a book from his pen dealing with his favourite subject should be both interesting and informative. As the author states in his preface, there has been no complete treatise on this subject since 1902, when Dr. Würdemann and Prof. Magnus brought out their book on "Visual Economics". The rapid extension of industry and the introduction of laws of compensation for industrial injury since that time have rendered a new study of the subject imperative. This is all the more true since the advent of the war, when men are being trained in new skills and trades, with the consequent increase of industrial injury. Moreover, this is the first book which deals extensively with the fundamental principles underlying medicolegal ophthalmology.

Although the author is an American, and, therefore, deals with ophthalmic economics as it is affected by American law, the subject matter of this book is so fundamental that it is worthy of study by ophthalmologists of all nationalities. This is particularly true of his chapters dealing with the responsibilities of medical and expert witnesses, mal-practice, the evaluation of

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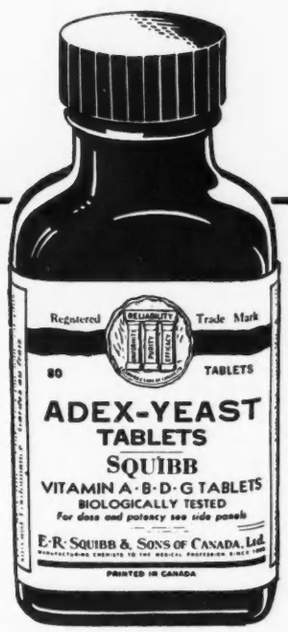

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visual disabilities, and the application of the visual efficiency computation to medicolegal practice. There is also a valuable chapter dealing with malingering and its detection. All in all, this volume will be a most readable and valuable addition to our ophthalmological libraries.

Microscopic Anatomy of Vertebrates. J. I. Kendall. 2nd ed., 342 pp., illust. $3.75. Macmillan, Toronto, 1940.

Responsibility for the 2nd edition of this work is undertaken by Professor Kendall alone, as Professor George G. Scott, the co-author of the original edition, has retired. In the new edition some text has been added, a few of the less helpful pictures in the original edition have been omitted, and many more useful illustrations have been inserted. The book is now arranged in a more systematic manner; each vertebrate sub-class is taken in order and its tissues are described. Sometimes these descriptions are rather brief, but the book aims at covering a wide field within a reasonably short space. It is an excellent textbook for students of zoology and as an introduction to the more specialized field of human histology.

Controlled Fertility: An Evaluation of Clinic Service. R. K. Stix and F. W. Notestein. 201 pp. $3.00. University of Toronto Press, Toronto, 1940.

This book is of value chiefly to persons specially interested in birth control. It is in no sense a popular text, and indeed will be well nigh incomprehensible to the uninformed reader. Its purpose is to assess critically the results of organized birth-control methods. It is perhaps not fully appreciated that 100 per cent success can rarely be claimed for contraceptive methods, even though applied under the instructions of a birth-control clinic. The intelligent co-operation of the client is essential, and the less intelligent the client, the more the liability to failure on the part of the method. One of the points brought out by the study is the high percentage of clients of the clinic who abandon the instruction given them in the clinic.

Probably a considerable number of persons who consult a birth-control clinic do so because of the failure of unguided contraceptive methods. It may be assumed that many of these people are also unusually fertile, and so present to the clinic a problem of unusual difficulty. The birth-control clinic clientèle cannot, therefore, be considered typical of the population at large.

The data, which furnish the basis for this volume, have been derived from the Birth Control Clinical Research Bureau of New York City, the oldest and largest contraceptive clinic in the United States. The authors, however, have no connection with the clinic. The senior author is Research Associate for the Milbank Memorial Fund, the junor author is on the teaching staff of Princeton University. The only prejudice which the authors admit to have had in approaching their problem was a belief that married couples were justified in limiting the number of their children.

From the detached nature of the study and the auspices under which it was carried out it can be safely assumed that this study is in fact a critical appraisal of birth-control clinic methods. For this reason birth-control enthusiasts should read it.

Public Health Administration in the United States. W. G. Smillie. 2nd ed., 553 pp. $4.25. Macmillan, Toronto, 1940.

Works on a subject as inclusive as public health administration are prone to divide themselves into two groups—those that are primarily informative and those that are designed to assist the health officer in the better conduct of his official duties. Dr. Smillie has found it possible to incorporate enough of the so-called informative material into his book to make it of value as a record of public health progress in the United States, without its losing any of its usefulness as a guide to the field officer.

While the procedures recommended are in keeping with accepted practice and modern in their approach they are presented without finality. If one were to be critical, it could be said that there is not sufficient emphasis on the value of accurate and adequate recording of time, money and effort expended. Such accounting is essential to the successful conduct of a community health program. The implied inclusion of an official interest by the public health administrator in the field of nutrition and its antithesis malnutrition is in keeping with the present trend.

There is an urgent need for a concise text on this subject, and the new edition of Dr. Smillie's book is strongly recommended to all those interested in the field of public health administration.

Chronicle of Crichton Royal. C. C. Easterbrook. 663 pp., illust. 25s. 9d. Courier Press, Dumfries, Scotland, 1940.

An admirable record of the greatest institution of its kind in Scotland by the eminent psychiatrist who was its superintendent for 30 years. Founded in 1833 by the widow of Dr. James Crichton, who had made a fortune in India and left the then enormous bequest of a hundred thousand pounds for some charitable purpose, it opened its doors six years later to some 120 patients. It now has accommodation for nearly 1,500. Beginning as a pioneer establishment for the humane and scientific treatment of the insane, it has always lived up to this ideal. An interesting feature of its statistics is the great increase of late years in the proportion of voluntary admissions.

Syphilis in Earlier Days. J. R. Whitwell. 90 pp. 5s. H. K. Lewis, London, 1940.

An excellent and concise review of the early literature. No entirely convincing record of pre-Columbian syphilis has yet been found in America or elsewhere, either in bone lesions or on paper, parchment or stone; but it has been the tendency of recent historians to suspect some obscure ailments in antiquity and the middle ages of having been syphilis, and to absolve our continent and the "Great Admiral" of responsibility for the pandemic of the Renaissance. Dr. Whitwell concludes "that this disease was no new one, but one that had existed from time immemorial".

Surgery of the Hand. R. M. Handfield-Jones. 140 pp., illust. $4.50. Macmillan, Toronto, 1940.

This book is written in large print and on a good type of paper, so that it is easy to read. The different subjects are followed through in a simple and consecutive way. The author must be congratulated on having the energy to complete the book during wartime conditions.

Prevention of accidents, first-aid treatment, and physical therapy are stressed. Pulp infections are discussed, and the author suggests incision at the site of infection where the infection is early; in later infections lateral incisions are recommended. The horseshoe incision quite rightly is condemned. One feels that too much stress is laid on the different compartments in the finger tip, and that generally speaking, less harm would be done if the teaching were to drain pulp infections by a small incision over the site of the infection. Lymphangitis is fully discussed, and excellent treatment recommended. It is doubtful if the fulminating type described should be included, because in all probability this is septicæmia from the beginning. The author recommends late repair of cut tendons, and, naturally, this is open to debate. One feels that the operative treatment to free tendons embedded in scar tissue and surround them with grafts of fat is recommended too highly. Other less frequently seen lesions are discussed. For the treatment of trigger-finger the author suggests that a plastic operation must be performed, either on the tendon or its sheath. Probably all of these are curable by a simple incision into the tendon sheath.

Everything considered, this book should be a valuable addition to the surgeon's library. It is much easier to read than many other books on the same subject, and its simplicity and clarity recommend it.

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Diseases of Workers: Latin text of 1713. W. C. Wright. 549 pp. $5.00. University of Chicago Press, Chicago, 1940.

This is the seventh in the series of Medical History publications of the New York Academy of Medicine, and makes available to English readers one of the great pioneer books, the first scientific study of occupational diseases. The older translations, 1705, 1746, etc., besides being rare and based on Ramazzini's less important first edition (1700), are very incomplete and defective; this one is scholarly and definitive, as one would expect from the translator of the "Contagion" of Fracastorius. The introduction and notes are most informative. Mrs. Wright, who is Professor of Greek at Bryn Mawr, deserves well of our profession.

Textbook of Medicine. Edited by J. J. Conybeare. 5th ed., 1131 pp. $7.25. Macmillan, Toronto, 1940.

This is the fifth edition of this well-known textbook. There has been re-writing of several sections, particularly on the sulfanilamide group of drugs; also a new chapter on congenital cystic disease of the lung. The book is sound and clearly written.

Obesity and Leanness. H. R. Rony. 300 pp., illust. $4.25. Macmillan, Toronto, 1940.

Here is a book which goes into the whole subject of obesity and leanness exhaustively. Almost six hundred references are made to the literature on metabolism. The chapter on caloric balance contains a good discussion of hunger mechanism. Why does the obese person eat independently of his caloric requirement? What is wrong with the mechanism that normally adjusts appetite to caloric output? What part of this mechanism is primarily disturbed—the peripheral neurogastric hunger apparatus, or its chemical, glandular or cortical control?

It may be a surprise to learn that "practically all investigators agree that the basal metabolism is within normal limits in the great majority of obese persons". The endocrine system and the nervous system each have a chapter, then fat, carbohydrate and protein metabolism are taken up in detail. Lipophilia is given a chapter. The rôle of heredity is discussed. "The ultimate problem of the inheritance of obesity and leanness is to find out which tissue or organ *Anlagen* carry the genetic factors that make for the fat content of the body. Are they inherent in genes of endocrine glands (and which endocrine glands) or of the nervous system, or the peripheral fat deposits? Or are there specific independent genes for obesity and leanness which are transmitted either alone or else in linkage with genes of endocrine or other anomalies"?

The clinical aspects of obesity and leanness, together with therapy for these conditions, are fully covered.

This is a book for anyone interested in metabolism, whether that person be an internist or a dietitian.

Venereal Diseases. E. T. Burke. 549 pp., illust. 30s. H. K. Lewis, London, 1940.

In this book the whole field of venereal diseases is covered in a fairly concise manner. Short chapters are devoted to the more unusual infections, *e.g., Trichomonas* which is called "*Trichomonas* Donne" infestation rather than *vaginalis* since the disease is seen in both sexes. Treatment is given in considerable detail, including the latest additions to armamentarium, such as the sulfonamides and artificial fever. Treatment is largely along accepted lines and is sound.

Some view points, while they may have much to commend them, are at too wide variance with accepted teaching to be advised for the beginner. The author explains the whole behaviour of syphilis on a lipoid concept. "The organism is an intense lecithin-globulin complex. It exhibits a marked predilection for the tissues of the host which, like itself, are rich in lipoids. Its favourite habitat is the perivascular lymph spaces of vessels associated with such lipoid rich organs and tissues."

Or again "the difference between the two sexes is a metabolic one and can only be expressed in terms of lipoids. One is forced irresistibly to the conclusion that the mildness of syphilis in the female is due to her high degree of lipoid richness. This may cause her to produce more of the protective lipo-proteolytic ferment and a higher proportion of it will be anchored to her tissues than to those of the male. They will thus be better protected from treponemal attack. "The female may legitimately on these grounds be regarded as the natural host of *T. pallidum*. She lives with the parasite in greater symbiotic amity than does the male. Syphilis does her less harm than it does her husband. She tends to become a carrier."

The bacteriology of gonorrhœa is well presented in line with the growing rise of cultural methods. Here, too, novel and fascinating views are expressed as to mutation forms and symbiosis of the organism that are not generally accepted. However, the imagination is sharpened.

Surgical Anatomy of the Head and Neck. J. F. Barnhill and W. J. Mellinger. 2nd ed., 773 pp., illust. $15.00. University of Toronto Press, 1940.

A second edition of this work has now been published. It shows some improvements over the first one; the illustrations are placed in closer proximity to the relevant text and several fresh ones have been added. But the work still remains a text-book written by an oto-laryngologist and bears the imprint of its origin on every page. Its outlook is more surgical than anatomical, and points bearing on oto-laryngology are fully discussed while other matters are ignored or given a cursory description. The cervical spinal column is not even mentioned, for instance, the temporo-mandibular joint is almost wholly omitted, and the lymphatic system is given only a few passing and brief references. The book contains a great amount of information of value to an oto-laryngologist but interspersed through this information is a considerable amount of trivial and exceedingly elementary matter such as would hardly be needed by a student of what purports to be an advanced practical text-book. The doggerel rhyme about the cranial nerves on page 698 is an outstanding example of these trivialities. Perhaps this information may not be so unnecessary in places where anatomy occupies a very subordinate position in the curriculum of many medical colleges. The book is well printed and illustrated, but some of the illustrations are more striking and ornamental than informative.

The Care of Psychiatric Patient in General Hospitals. F. G. Ebaugh. 79 pp. $1.00. American Hospital Association, Chicago, 1941.

This timely little volume was prepared as a study publication of the Council on Profession Practice of the American Hospital Association, to focus attention upon the obvious need for greater interest in psychiatric states upon the part of those who staff general hospitals. Psychiatry is now regarded as a fundamental of general medical practice, and more general hospitals should have psychiatric divisions. It is pointed out that such an arrangement is better for the patient and for the medical staff, it provides additional highly desirable educational features for the nurses and interns, and is not the serious economic or administrative problem for the hospital which is commonly thought. Chapters are included on organizational requirements, on methods of psychiatric study and on principles of management. This study should stimulate interest in this desirable development.

BOOKS RECEIVED

Minor Surgery. R. J. McNeill Love. 370 pp., illust. 12s. 6d. H. K. Lewis, London, 1940.

International Clinics. Vol. 1, N.S. 4. Edited by G. M. Piersol. 304 pp., illust. $3.00 a vol. J. B. Lippincott, Montreal, 1941.

Handbook of Anæsthetics. Revised by R. J. Minnitt. 5th ed., 364 pp., illust. $3.75. Macmillan, Toronto, 1940.